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INTEGRATIVE FUNCTIONS OF THE CEREBRAL CORTEX

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Bubnoff and Heidenhain (1881) formulated the general principle that in investigations of the physiology of the nervous system every conscious process must be ruled from consideration unless it can be translated into objective terms. Pavlov (1927) adopted the same view and has consistently maintained that "there is no need for the physiologist to have recourse to psychology." From the standpoint of explanatory formulations, the validity of this principle cannot be seriously questioned. Psychological studies have resulted in the formulation of many generalizations, but attempts to build up systems based on "psychic causality" have not provided a satisfactory basis for a science. It is now increasingly, if not universally, admitted that the causal relations underlying these generalizations are to be sought in the activities of the brain. There are, however, many facts concerning the behavior of the organism which at present are expressed only in psychological terms and which must nevertheless be considered in any attempt to describe the activities of the brain or to understand the general principles of its organization.

Physiological theories of cerebral function have been derived in large part by inference from studies of nerve-muscle or of spinal preparations, lacking those very traits of behavior (learning and intelligent adaptation) which characterize the animal with intact nervous system and which are of primary importance in all its normal behavior. For all studies of nervous integration the correlation of excitation and reaction has been the most valuable research tool available. Direct measurements of electrical changes and the like have revealed something of the nature of the propagated disturbance, but even the concept of the reflex is based upon the stimulus-response relations within isolated segments, rather than upon any direct observations of what goes on within the

integrating system (Skinner, 1931). A large part of the data of psychology is based upon attempts at exactly the same sort of analysis of stimulus-response relationships. The chief method of physiological investigation of the nervous system is therefore not logically prior to that of a behavioristic psychology. The greater scientific importance of the physiological studies lies rather in the simplicity of the conditions imposed and the consequent greater probability of a correct analysis of the data.

This very simplicity of the situations studied may result in a failure to consider problems which are fundamental for the behavior of the intact organism. Psychological studies reveal many instances of behavior which seem to involve principles of integration not thus far established for the activities of the decerebrate preparation and which seem out of harmony with concepts of neural integration derived from studies of lower centers. Boring (1932) has stated the problem clearly.

> The physiologist holds to the faith that the brain, being made up of neurons, is capable only of that excitation which is the sum of the excitations of many neurons, and that these central neurons obey the same laws and are excited under the same limitations as apply to the peripheral neurons which have been experimentally studied. To this article of faith the psychologist sometimes opposes another belief, that the organization of cerebral excitation corresponds to the organization of phenomenal experience.

That there is any essential contradiction between the established facts of nerve conduction and the phenomena of complex behavior cannot be maintained by anyone interested in the progress of natural science, but the extent to which the concepts of cerebral function derived from studies of lower centers are adequate to account for the facts of behavior can be determined only by a more complete study of the problems of behavior and by direct experimental tests of the explanatory concepts.

Clinical observations and experimental studies with animals provide the two principal sources of more direct data upon the activities of the cerebral hemispheres. The clinical facts are exceedingly complex and the possibilities of anatomical correlations distinctly limited. With animals the anatomical control may be far more perfect, but in the earlier work this advantage was counterbalanced by the difficulties of interpreting behavior. The past thirty years have seen marked development in the methods for studying animal behavior, of which little advantage has as yet been taken for neurological studies.

The object of the present review is to formulate some of the significant problems on the borderline between psychology and neurology

which may be attacked by experimental methods now available for study of animal behavior, and to summarize experimental data which bear most directly upon these problems. The subject of cerebral localization has been very adequately treated by Hines (1929) and by Graham Brown (1927) and will be touched upon here only where it bears upon the problems of cerebral integration. Klüver's review of the literature on visual disturbances (1927) and Goldstein's discussions of aphasia (1923, 1924) deal with clinical aspects of many of the problems discussed here.

LIMITATIONS AND POSSIBILITIES OF METHOD. The development of techniques for the study of animal behavior since the first quantitative work of Thorndike in 1898 has opened many possibilities for correlated studies of behavior and neurology. Methods are available for the measurement of activity (Slonaker, 1908; Szymanski, 1920; Richter, 1922, 1927), for a comparison of the effectiveness of incentives (Moss, 1924; Warden, 1931), for estimation of individual differences in certain reactions termed emotional (Yerkes, 1913; Stone, 1932), for determining sensory capacities by the conditioned reflex method of Pavlov (1927) and the discrimination method of Yerkes and Watson (1911), for measuring the rate of acquisition of many varieties of habits, with a number of standardized tests worked out chiefly for the rat and monkey, and for direct adjustment to many situations, comparable to problems requiring reasoning and understanding of relations by man (Warner and Warden, 1927; Yerkes and Coburn, 1915; Köhler, 1921; Jacobsen, 1931; Klüver, 1931).

The chief difficulties in the studies of behavior arise from uncertainty as to the validity of the tests, a handicap shared almost equally by animal and human studies. The development of quantitative psychological tests for various activities is bringing about a change in the fundamental conceptions of the organization of psychological traits which is the most significant phase of current work. In attempts to measure individual differences, it has been a general experience that the activities or traits which were grouped together in the classical and popular categories of psychology (perseverance, emotionality, intellect, and the like) often show a degree of independence which is inconsistent with the assumption that they are products of a common causal agent. Groups of activities do show a high degree of intercorrelation, indicative of a common determining factor, but these groupings are so far from coinciding with the older classification of traits that it has seemed better to investigators to designate them by letters, than to attempt to fit

them into the older classification. Thus we have Intellect CAVD (Thorndike, 1926), traits *g*, *c*, *w*, etc., (Spearman, 1927) instead of the familiar terms. A test may correlate with *g*, which in turn correlates with ability in handling school subjects, but such ability may be independent of ability in handling mechanical problems and both independent of ability to make an intelligent adjustment to social situations.

This means that the validity of the tests used must be established before their results justify any generalizations: that is, the functions which they are intended to measure must be defined and it must be demonstrated that the tests actually do measure the functions. Bianchi (1922) and others who have reported intellectual defects after frontal lobe injury have stressed silly behavior, Witselsucht, which is perhaps an inadequacy of social adjustment, whereas Feuchtwanger (1923) and others who report normal intelligence have used tests which probably correlate with the group termed *g*. The controversy has arisen at least in large measure from a failure to recognize the probable diversity of the functions included under the popular term "intellect" and the inadequacy of the tests to measure all of these functions.

In experimental studies with animals the validity of the tests comes still more in question, so that it is scarcely safe to say that a test measures anything more than performance in the test itself. There is a high correlation in performance in certain tests, such as the learning of different mazes (Stone and Nyswander, 1927; Tryon, 1931; Leeper, 1932) which justifies some generalization concerning maze-learning ability, but even here we do not know whether we are measuring fixation in memory (the ekphorie of Semon, 1908), or some process akin to the solving of puzzles (insight, Köhler, 1929).

On the physiological side, the methods for direct study of cerebral function present equal difficulties of another character. We are still largely restricted to methods available to the workers of the nineteenth century. The direct measurement of electrical changes in the cortex with the development of amplifying and recording instruments may revolutionize cerebral studies, but thus far has not given indication of differentiae which are useful for interpreting cerebral mechanisms (Travis and Herren, 1931; Bartley and Newman, 1931). Whether this is due to inadequacies of technique or to some fundamental property of the cortex remains to be determined, but leaves us still with stimulation and extirpation methods as the chief means available for direct study of cortical function.

Stimulation of the cortex in animals permits the designation of some

areas which seem to be more intimately concerned with movements than are other areas, and in the hands of Sherrington and his co-workers has revealed something of the patterns of organization elaborated at different levels and of the mutual facilitation and inhibition of different areas. Stimulation of conscious human subjects further reveals cortical fields within which sensory elaboration occurs. The strychninization method of Dusser de Barenne (1916) has given some similar data for animals. These methods, however, seem limited to revealing rather isolated functions, and extirpation remains the principal method available for gathering data upon the rôle of the cortex in the more complex adaptive reactions of the animal to its environment.

The interpretation of results obtained by the extirpation method presents peculiar difficulties. Following operations, symptoms may arise not only as a result of the simple absence of functional tissue, but also from derangement of the functions of the remaining tissue as in shock, general circulatory and nutritive changes, physical or chemical effects of necrotic or scar tissue, and the indirect depression of diaschisis. As Monakow (1914), Pavlov (1929), and many others have pointed out, the immediate symptoms are an unreliable index of the functions of the area destroyed. Upon the just ascription of symptoms to these various agencies depend important points in the interpretation of cerebral functions. Surgical shock, circulatory changes, and irritation may be controlled with considerable certainty by following changes in symptoms over a sufficiently long time, while precluding the possibility of relearning or of normal forgetting. The control of diaschisis is more difficult since the concept is not very clearly defined.

Diaschisis and Re-education. Von Monakow's theory of diaschisis puts serious difficulties in the way of any attempt at experimental analysis of cerebral mechanisms. Briefly, the theory embodies the following points. 1. Destruction of a cortical area may result in symptoms which are due to the withdrawal of facilitation from some other area and the resultant inadequacy of functioning of that facilitated area. 2. Areas subject to such diaschisis effects recover their functions spontaneously, but no limit can be set to the time required for such recovery. 3. Only such functions as are permanently impaired can be ascribed to a destroyed area.

This theory casts doubt upon the validity of any experiment involving re-education unless it can be shown that the functions studied do not recover spontaneously but do recover under the influence of training. Adequate controls of spontaneous recovery have been reported in few

cases. Oden and Franz (1917) destroyed the precentral gyrus in three rhesus monkeys, left one untreated, gave the second passive massage, and the third compulsory use of the hemiplegic arm, repeating the experiment with the second motor area after recovery from the effects of the first operation. They found scarcely any spontaneous recovery, whereas compulsory use was followed by nearly complete recovery within a few weeks. Lashley (1926) varied the interval subsequent to destruction of the area striata at which retraining in the habit of reacting to light versus darkness was begun. One group, started on the seventh day after operation, had practically reacquired the habit by the fourteenth day. A second group, started on the fourteenth day, began at the level of efficiency shown by the first group on the seventh day. As in the study of Oden and Franz, retraining produced recovery which did not occur spontaneously in the absence of special training. A number of experiments, such as those of Trendelenberg (1915), reveal recoveries ensuing promptly upon the forced use of paralyzed organs, after long periods in which no improvement was observed. A good bit of material in human re-education indicates the same dependence of recovery upon training, but lacks rigid controls (Franz, 1905; Graham Brown and Stewart, 1916). The evidence seems conclusive that some functions lost through cerebral injury may be recovered as a result of special training and that these functions are not recovered spontaneously in the absence of training. Two questions at once follow this fact: by what neural changes is such recovery brought about and what are the limits of recovery for any function?

The mechanism of recovery through re-education. The manner in which the retraining is effective offers in each case a special problem. There seem to be at least three possibilities which must be tested: 1. Learning to get along without the lost functions. 2. Vicarious assumption of the functions by neural structures not previously utilized in the functions. 3. A reorganization within the system of which part has been destroyed, such that there is compensation for the loss.

The first of these possibilities is illustrated by the recovery from circus movements reported by Luciani (1907) after cerebellar unilateral lesions. The dogs learned to walk in a straight line by altering the postures of the fore and hind legs as might an animal with a mechanically imposed spinal curvature. Maze running of rats with extensive cerebellar destruction (Lashley and McCarthy) in which the animals practically rolled through the maze is a similar instance. Bethe (1930) has reported studies of reorganization of gait following amputation of one or

more limbs in invertebrates and in mammals. He holds that, with the removal of the limbs there is an immediate reorganization of the sensory-motor system such that adequate walking movements, which have no counterpart in the integration of the normal animal, are made. In his cases, substitute activities are obvious; the problem is to determine whether they are learned, or acquired by some spontaneous central reorganization.

In studies of less objective or overt behavior it is more difficult to detect substitute activities or to rule them out as a factor in recovery of functions. The question has been raised (Goldstein, 1931) whether injury to the nervous system is ever followed by a genuine restitution of functions or whether all cases of recovery under re-education do not represent the adoption of some roundabout method of achieving the same end, such as in Bethe's studies or in the development of pseudo-fovea (Fuchs, 1921). It is very difficult to obtain conclusive evidence upon the question, for the answer in any specific case depends upon opinion as to the exact nature of the defect. Recovery from cerebral paralyses with acquisition of the use of specific muscles seems to constitute the best evidence for genuine restitution, but even this is not crucial, if the initial loss of use is ascribed in part to sensory defect. Loss of habits resulting from cerebral injury and their subsequent formation at a rate and with objective performance identical with their pre-operative formation argue for a restitution rather than a substitution of functions. Formation of motor habits has been reported by Graham Brown (1916), Trendelenberg (1915), and Lashley (1924a) after destruction of the motor cortex. Lashley (1922) found that after the complete destruction of the area striata, habits based on the discrimination of light and darkness were abolished but could be reformed at exactly the same rate as the original formation in normal animals, and seemed to be performed in the same way.

The clinical literature includes many cases of recovery from amnesias with retraining (Franz, 1905, 1924; Head, 1926) and of improvement in other functions (Brown and Stewart, 1916), which can be understood only in terms of some genuine restitution of functions.

The problem of vicarious functioning. It has generally been assumed that the recovery of functions lost after destruction of cerebral areas is due to the assumption of the functions by other cerebral areas which did not originally mediate the activities. Fritsch and Hitzig (1870) first suggested this hypothesis as a possible explanation of the recovery of motor control in the dog after extirpation of the stimulable cortex of

one hemisphere, assuming that the motor cortex of the other hemisphere assumed the lost functions. They put the hypothesis to experimental test, removing the remaining motor cortex in a second operation, and obtained the usual crossed paralysis with no recurrence of symptoms on the side of the second operation. This negative result has been confirmed by a number of investigators both for the dog (Carville and Duret, 1875) and for primates (Trendelenberg, 1915; Oden and Franz, 1917; Leyton and Sherrington, 1917; Lashley, 1924a). In no case has a recurrence of the motor symptoms produced by the first lesion been reported to follow the destruction of the corresponding area of the opposite hemisphere.

A few tests have dealt with the assumption of functions by adjacent parts of the same hemisphere. Franz (1907) reported loss of latch-box habits after destruction of the frontal pole in the cat with relearning and a second loss following destruction of an area just back of the first lesion. He did not control these results by lesions in other parts of the cerebrum and recent work suggests that loss of such habits may follow lesions anywhere within the hemispheres, so these experiments cannot be accepted as demonstrating vicarious function of an adjacent area. All other similar experiments have given negative results. Leyton and Sherrington (1917) destroyed small areas in the precentral gyrus of chimpanzees and after recovery from the local paralyses extirpated surrounding regions and portions of the postcentral gyrus. In no case did they get significant recurrence of the original paralysis. Lashley (1922) destroyed the area striata in 14 rats. This lesion invariably causes loss of pre-existing habits based on the discrimination of light and darkness. He next trained the animals until accurate discrimination of light and darkness was obtained and then destroyed one-third of the remaining cortex in each animal, covering all parts of the cortex in different animals of the series. Nearly perfect retention of the habit followed lesions in all parts of the remaining cortex. No limited part of the remaining cortex assumed the function of the lost striate area.

Arguing from the embryology of the motor cortex that the caudate nucleus might have a related function and be capable of vicarious substitution for the motor cortex, Lashley (1924a) removed the precentral gyrus in a cebus monkey and after improvement in the consequent paralysis destroyed the greater part of the caudate and the head of the lenticular nucleus. A typical lenticular syndrome resulted but without recurrence of the hemiplegic symptoms.

In several experiments with nerve suturing, the motor nerves have

been transferred from one side of the body to the other (Bethe, 1905; Osborne and Klivingston, 1911; Kennedy, 1913). On later stimulation of the motor cortex, Bethe obtained co-ordinated movements of all the joints of the limb although different segments of the limb were innervated from different sides of the cord. In other investigations stimulation of the motor cortex after nerve crossing has given evidence only of the connection of the crossed nerves with the originally contralateral motor area. These experiments have been cited as evidence for vicarious functioning, but the reorganization of co-ordinations in such cases does not necessarily involve anything more than such changes in function as underlie all learning. In fact, the experiments do not even demonstrate a change in the functions of the motor area, since we do not know its normal function in the movements of progression. A reorganization of some portion of the motor system is implied but this presents a somewhat different problem from that of vicarious assumption of functions by centers which have not previously been concerned in the functions.

In every case where a localized area functioning vicariously has been sought, the experiments have given only negative results. The number and variety of such experiments is not great enough to justify a denial of the principle of vicarious functioning, but does point to the necessity for further experimenting before the use of the principle as an explanation of recovery can be accepted.

The alternative to vicarious functioning is a reorganization within a dynamic system of which only a part has been destroyed. Such an hypothesis has been proposed as a substitute for the doctrine of specific centers in spinal integration. Bethe (1931), citing his own work and that of Buddenbrock (1921) on spontaneous reorganization after amputation of limbs in arthropods, assumes that co-ordination in walking is not due to specifically localized centers but is the product of relative intensities of excitation, aroused by muscle tensions, within a relatively undifferentiated system. Change in co-ordination follows spontaneously upon any change in relative masses of excitation within different parts of the system. Direct evidence in support of such a theory is lacking.

The limits of recovery. Some improvement in function seems possible after any injury in the central nervous system provided adequate means of retraining are used, but the limits to improvement set by lesions of various sorts have rarely been tested, and few generalizations are possible. There are marked interspecies differences, as in severity of

paralysis (Rizzolo, 1930) so that generalization from one form to another is unsafe.

In interruption of spinal tracts, the residual sensory defects seem always more severe than the motor, at least in forms below man, although there are always some residual motor symptoms. With cerebral lesions, sensory defects also present the least possibility of improvement. Scotomas from extensive lesions to the primary visual areas are permanent in many species (rat, Lashley, 1931c; dog, Minkowski, 1911), and such improvement as appears is due to substitution of function (Goldstein, 1931). Defects in other less highly differentiated areas or in areas with bilateral representation of the receptors, as the somesthetic, show a greater capacity for improvement (Foerster, 1930). Pronounced improvement after destruction of the motor cortex is reported for all forms from the rat to man, but even in the rat there are permanent residual symptoms such as determination of the preferential use of one forepaw, after unilateral lesion (Peterson, 1931).

For functions farther removed from the sensorimotor level the possibilities of recovery are greater. Limits of improvement seem to be set by the extent of injury and by the complexity or psychological difficulty of the problem (Lashley, 1929a, rat; Jacobsen, 1931, monkey; von Monakow, 1914, man). The meager data on re-education do not permit any wide generalizations. The difficulties of interpreting the results of extirpation experiments and the more essential controls of disturbing factors are illustrated by the foregoing discussion. Few investigators have attempted any systematic study of such factors and the great body of work upon cerebral localization is consequently inconclusive. The conclusions drawn in the following sections must be regarded as tentative, pending further analysis of the rôle of diaschisis and of general circulatory and nutritive disturbances in the production of postoperative symptoms.

Cerebral function in instinctive behavior. The majority of problems of cerebral function center around activities which are known to have been acquired through some learning process and the opinion has been expressed that the cerebrum is not essential for the performance of any unlearned or instinctive activity (L. Morgan, 1912). Very few studies have dealt with the rôle of the cortex in instinctive behavior and the problem is greatly complicated by the difficulty of ruling out an element of learning in the acquisition of all activities (see, for example, the analysis of the pecking reaction of chicks by Breed, 1911, and Bird, 1926).

Many of the reactions which are judged to be instinctive persist in the decorticate animal. Rogers (1922) finds that the activities of mating and rearing the young by pigeons are carried out in a nearly normal manner after decerebration. Shaklee (1921) reports that decerebration abolishes the drinking reaction of chicks but leaves pecking undisturbed. He interprets this in terms of later phylogenetic acquisition of drinking. In decerebrate mammals the range of activity is less than in birds. All writers (Goltz, Rothmann, Zeliony, de Barenne) have reported loss of feeding reactions (taking food into the mouth and passing it back to the pharynx) after decerebration, with later recovery in most animals.

Mating reactions, at least in male dogs, seem to be permanently abolished (Rothmann, 1923). Instinctive reactions other than sexual have scarcely been studied in mammals. Patterns of movement and visceral reactions corresponding to emotional behavior of the intact animal have been reported in decerebrate cats (Bard, 1928) and dogs (Rothmann, 1923). Sleep is normal except for lack of diurnal rhythm (Kleitman and Camille, 1931).

The sex activities of the rat are the only mammalian instincts which have been subjected to careful analysis from the standpoint of origin, adequate stimulus, and other determining conditions (Stone, 1922). Stone has found that destruction of large areas of the cortex in the rabbit produces no disturbance in mating behavior (1925b). I have observed that nearly complete decerebration in the male rat abolishes the reactions to the female in heat. Lack of recognition of the adequate stimulus seems to be the primary factor in the loss, but it is also possible that the poor physical condition of the animals suppresses the sexual drive (Stone, 1924, 1925a).

Unpublished observations by Stone and the writer indicate that the more complicated activities involved in rearing the young (nest building, collecting and cleaning the young, nursing, etc.) are interfered with by cerebral lesions and that the behavior is progressively simplified with increasing size of lesion.

The evidence seems quite conclusive that such complex integrations as those involved in recognition of the female in heat and the selection of nest material develop independently of individual experience and there are indications that in mammals they cannot be performed in the absence of large portions of the cerebral hemispheres. This implies that some instincts, which seem to be those requiring accurate differentiation of stimuli, are dependent upon cortical mechanisms. Whether this

dependence implies that the necessary integrations are carried out within the cortex, or only that severe diaschisis of subcortical centers after decerebration persists indefinitely, remains uncertain.

CEREBRAL FUNCTION IN LEARNING. The importance of the cerebral hemispheres for the learning process is obvious from a large number of experiments, but little has been revealed concerning the nature of its activities in learning. The demonstration of the formation of complex habits in arthropods (Turner, 1913; von Frisch, 1914; Schneirla, 1929), molluscs (Goldsmith, 1917), and perhaps still lower invertebrates shows that typical cerebral structures are not necessary for learning. Nor is there any evidence that the rate of acquisition of the simplest associations increases with the development of the vertebrate nervous system. On the other hand, the range of activities and the complexity of relations which can be combined in habits increases pari passu with development of the cerebral hemispheres (Lashley, 1929b).

Burnett (1912) attempted to train decerebrate frogs in a simple maze which was easily learned by normal animals. His results were entirely negative. His operations may have involved injury to the optic lobes. In birds, several investigators report the acquisition of simple habits after removal of the cerebral hemispheres, if the striate nuclei are retained. Treves and Aggazzotti (1901) trained a decerebrate pigeon to find its way back to its perch and found that the habit was retained for several weeks without practice. Rogers (1922) observed the combination of isolated sexual reactions into the mating cycle in decerebrate pigeons and failed to get the integration after injury to the hypostriatum. Gemelli and Pastori (1930, 1931) trained fowls in color-discrimination and report a partial survival of the habit after decerebration with further improvement under practice and a subsequent, unexplained deterioration.

With decerebrate mammals the results have been for the most part negative or difficult to interpret. Improvement with practice in a number of simple activities has been reported, but with these it is difficult to determine whether the improvement represents learning or the spontaneous recovery of reflexes. Goltz (1892) found that following operation food must be placed in the pharynx to induce swallowing but that gradually the dog came to pass food back from the jaws and ultimately to seize it when placed in contact with the lips. Rothmann (1912) has reported similar observations. He also described an experiment in which the forefeet of his dog were placed on a chair and the chair drawn along the floor. At first the animal made no effort to

follow. With practice he "learned" to step with his hind feet, following the movements of the chair. In later experiments his dogs came to leap over a hurdle, and sit up when supported against a wall (1923). The observations of Buddenbrock (1921) and of Bethe (1930) suggest that this sort of adaptation may be due to changes in postural tonus which are not comparable to learning. These experiments, involving merely restitution of primitive functions, are of doubtful value as evidence of learning by lower centers, for, as Rothmann pointed out, the improvement may represent only the recovery of reflex mechanisms from a depression following the operation, with no involvement of associative mechanisms. On the other hand, they may be instances of genuine learning.

Head and Riddoch (1917) report an apparent conditioning of the bladder reflex in patients with complete section of the spinal cord, but the same objection applies to this evidence as to restitution of functions in decerebrate animals.

Ingebritsen (1932) attempted to establish conditioned reflexes in the hind legs of rats with spinal sections. He used animals with complete section in the thoracic region and others with two hemisections separated by about four spinal segments, attempting to associate an avoiding reaction of the foot with light contact on the thigh. No indication of conditioning appeared in animals with complete transection. Unstable and irregular reactions appeared in animals with double hemisection, which indicated an increased excitability to tactile stimuli after protopathic stimulation.

Few systematic attempts to establish more complex habits in decerebrate mammals have been made. Goltz (1892) tried to train his dog to back out of a stall, but gave up training after a few unsuccessful trials. Kleitman and Camille (1931) interpret the irregular periods of activity in decerebrate dogs to a failure to form habits of diurnal activity. In a series of papers Zeliony (1913) reported negative results in attempts to establish conditioned reflexes in decerebrate dogs, but more recently Poltyrew and Zeliony (1929, 1930) have succeeded in establishing a conditioned motor reaction to the sound of a whistle and also a differential reaction to another sound, and in two cases a further response to the lighting of an electric lamp. Necropsies of the animals have not been reported, but the descriptions of operations indicate that at most only small basal portions of the temporal lobe remain intact. The authors find that very strong stimuli are required to establish the conditioned reaction.

From the results with decerebrate animals we can infer little as to the modifiability of subcortical mechanisms in the intact animal. It may be that the removal of the cortex decreases the plasticity of lower centers by withdrawing some nonspecific facilitation, which under normal conditions permits learning without actually contributing to the specific integrations. Such a view is supported by the results of Ingebritsen (1932) on learning after double hemisection of the cord, and by the observations of Lashley (1926, 1929a) that the formation of some habits is closely dependent upon the mass of cortical tissue available, irrespective of its specialized character. Crucial experiments are lacking.

The reduction of automatized habits to subcortical levels. There is a widespread belief (Morgan, 1912; Franz, 1907) that continued practice results in the formation of subcortical associative connections such that habits which originally involved the cortex are carried out wholly by lower centers. The belief is based by Morgan on the following argument: all cerebral activities are conscious; long-practiced habits become unconscious or automatic; therefore they are no longer executed by cerebral mechanisms. The major premise is questionable or meaningless and the argument is not valid. The clinical evidence sometimes advanced in support of the claim that old habits survive injuries which abolish more recent ones is not conclusive because the activities compared differ in many other respects than recency of acquisition. Lashley (1921a) has attempted to test the question experimentally. He gave rats 1200 trials of overtraining in a simple habit of reacting to light. With this amount of training the behavior of the animals indicated automatization. Removal of the striate area of the cortex resulted in a recoverable loss of the habit precisely as in animals without overtraining. This is the only direct evidence bearing upon the question and opposes the doctrine of reduction of automatized habits to subcortical levels.

The conduction pathway in habit. On the assumption that the habit mechanism consists of definite and anatomically localized reflex pathways from receptor to effector, a few attempts have been made to trace such paths through the nervous system. Lang and Olmstead (1923) established an association between an auditory stimulus and an avoiding reaction in the left hind leg in dogs. After section of the right half of the cord, the reaction did not reappear on recovery of motor control of the hind legs, but could be re-established by retraining. The authors conclude that cutting of the sensory path for pain abolishes the reaction to auditory stimulation, and speculate concerning the necessity that the entire unconditioned reflex arc remain intact in order that the habit be

maintained. They did not, however, control the normal loss of such reactions through lapse of time, or allow sufficient time without retraining to eliminate a general depression from the operation as possible causes of the loss of function. The fact that the conditional respiratory reflex persisted suggests that depression of motor centers below the lesion was an important factor in their results. Lashley and Ball (1929) found survival of orienting control of the limbs required for maze-running after cervical section of the entire dorsal or of both lateral funiculi of the cord, and Ingebritsen (1932) obtained similar accurate orientation after a double hemisection of the cord at the second and fifth cervical levels, in which no more than a small portion of the tracts of the ventral funiculus remained uninterrupted.

Our most complete experimental data upon the afferent paths in learning and maintenance of habits are derived from studies of vision in the rat (Lashley, 1920, 1922, 1924b, 1926, 1929a, 1930*a*, 1931c; Freeman and Papez, 1930; Layman, 1931). The principal findings are briefly the following:

1. The habit of entering an illuminated and avoiding a darkened alley in the Yerkes discrimination box is formed with equal rapidity by normal animals and by animals lacking the striate area, or any other part (up to at least 60 per cent) of the cerebral cortex.

	Trials	*Errors*
Average of 98 normals	131	43.8
Average for 113 animals with extensive to complete destruction of area striata	123	40.6

2. Destruction of the striate areas in animals previously trained produces complete amnesia which does not recover spontaneously. Destruction of other parts of the cortex, even adjacent to the striate areas, does not disturb the function.

3. Animals with postoperative loss relearn the habit as rapidly as do normal animals.

4. The amount of training required is closely proportional to the amount of tissue destroyed, provided that there is some invasion of the lateral portions of both striate areas (correlation ratio equals 0.84).

5. Partial interruption of the optic radiations does not produce a proportionate loss of the habit.

6. When the habit is formed in the absence of the striate areas, subsequent destruction of any third of the remaining cortex does not seriously disturb the habit.

7. Animals trained in this habit with one eye blindfolded discriminate correctly when the blindfold is transferred to the other eye. This transfer takes place as readily in the absence of the striate areas.

8. Injuries to the superior colliculi retard the formation of this habit, somewhat in proportion to the extent of injury.

9. The formation of habits based upon pattern vision is not retarded by destruction of the colliculi.

10. Complication of the habit by requiring the discrimination of two lights approaching threshold difference results in a marked slowing of initial learning in animals lacking the area striata, although their threshold for brightness *may* be as low as that of normal animals.

11. Destruction of the striate areas in animals previously trained in this habit results in complete amnesia. Partial destruction of the areas sometimes seems to abolish the discrimination of two lights without markedly reducing accuracy in reacting to one light alone.

12. The degree of disturbance in learning involving two lights is somewhat proportional to the extent of destruction of the area striata, as shown by the following correlations:

	Correlation wi extent of lesion
Errors in learning reactions to two lights	0.58 ±0.10
Difference threshold	0.49 ±0.09
Postoperative retention	0.65 ±0.10

13. Interruption of the optic radiations as they enter the external capsule from the lateral geniculate bodies permanently abolishes all reactions to discrete visual objects, but does not interfere with the formation of the reaction to light versus darkness.

14. Destruction of the lateral portion of both striate areas permanently abolishes all pattern discrimination.

15. Destruction of the median portions of the striate area or of any other cortical fields does not interfere with the formation of habits based on discrimination of patterns.

16. Lesions in the median portion of the striate areas produce an amnesia for habits based on pattern discrimination, which may be reacquired by training. Lesions to other cortical fields do not produce such an amnesia (unpublished data).

17. Animals trained on visual patterns react on the basis of the relative attributes of the stimuli, reacting at once to similarities when there is no identity of retinal elements stimulated.

These results embody data upon both defects of vision and disturb-

ances of memory, and, as has proved true for clinical material also, it is difficult to disentangle these two aspects of the problem. The habit based on the discrimination of light and darkness shows least dependence upon the cortex. It is formed at normal rate in the absence of the striate area or of any other portion of the cortex (tested to 60 per cent), or even after a probably complete interruption of the optic radiations which abolishes all capacity to differentiate the position of objects within the visual field. This fact, taken together with the retardation from injuries to the superior colliculi and the formation of such habits in decerebrate dogs (Poltyrew and Zeliony, 1930), indicates that the associative mechanism for the habit lies in the subcortical structures. When the habit is formed in normal animals injury to the striate areas results in its loss, with the rate of relearning proportionate to the extent of injury. This loss is not due to general shock, since equal injuries in other parts of the cortex do not disturb the habit. It cannot be ascribed to localized visual defects such as scotoma, since there is no evidence that these in man necessarily involve amnesia or that the capacity to make discriminations of light and darkness is abolished in those parts of the visual field which are not included in the scotomatous area. It cannot be ascribed to a change in the criteria of discrimination (as from reaction to a definite visual form to reaction to simple luminosity), for under the conditions of this experiment it is practically impossible to establish a visual discrimination of pattern in normal animals and the formation of a habit based on the simplest spatial attribute of the stimulus lights, relative size, requires from five to ten times as long training as to obtain a habit to relative brightness. The regularity of effect of extent of lesion indicated by a correlation coefficient of 0.84 indicates that the various parts of the area striata have an equal function in preserving the residual traces of the habit mechanism which contribute to the shortening of retraining (see p. 133). These results have been interpreted as indicating one of two alternatives: either that in the learning of this habit in normal animals the cortex participates by the development of some nonspecific facilitative effects upon the lower centers, and that the specific integrations between receptors and the motor systems used in orientation are not contained in the cortex itself; or that the integrations of the habit involve a reorganization of the entire visual system without the local development of specific integrative connections.

The data upon discrimination of two lights cannot be interpreted because we have no evidence concerning the effects of interruption of the

optic radiations or of destructions in the anterior portions of the cortex upon this function.

For pattern vision it seems clear that the discrimination of the gross visual characters of objects requires some cortical connections, but can be mediated by the frontal portions of the cortex. This part of the system can mediate reactions to the relative position of discrete objects within the visual field but fails to distinguish between surface area and luminosity. The clear differentiation of spatial attributes of the stimulus is dependent upon the striate areas. There is no indication that any other portions of the cortex than the striate areas are concerned in the performance of habits based on pattern discrimination. Data on postoperative amnesias for this type of habit are as yet incomplete but from results so far obtained it seems clear that the habits are disturbed only by lesions within the striate area and there are indications that the habits may survive the destruction of any part of the visual cortex up to at least 50 per cent in both hemispheres.

Such data are by no means adequate to solve the problem of the mutual relations of cortex and lower structures in learning, but they suggest that there may be both general facilitative effects and specific integrative relations involved. They show that the concept of simple conduction pathways from receptor to the cortex, with the establishment there of an integrative pattern of neuron connections, is a quite inadequate picture of the afferent mechanism.

Attempts to trace the path of associative reactions within the cortex have been largely confined to the motor cortex as the most plausible point of exit. Wagner (1905), Bechterew (1916), and Gierlich (1913) have maintained that formation of motor habits is impossible after destruction of the motor cortex. Pike and Chappell (1930) have more recently reported failure in attempts to train animals (cats) in a motor habit after small injuries in one motor area. Failure in these cases may have been due to the fact that the lesions were unilateral, since Trendelenberg (1915) and Oden and Franz (1917) have shown that recovery of one paralyzed limb is unlikely so long as the animal has free use of the other.

Isolation of the motor cortex from surrounding areas has given conflicting results. Marique (1885) and Exner and Paneth (1889) reported symptoms after circumsection of the area identical with those following excision. Schäfer (1901) found normal control of movement in one case, which was not controlled histologically.

Starlinger (1895) trained a dog to give his paw after interruption of both pyramidal tracts. Rothmann (1917) and Graham Brown (1916) report formation of motor habits after destruction of motor areas or pyramidal tracts. Trendelenberg (1915) taught a dog to give his right paw after total extirpation of the left cerebral hemisphere. Pavlov (1927) reports the establishment of conditioned reflexes after removal of all of the motor areas in dogs. These authors, dealing with learning after extirpation, have been inclined to regard the motor cortex as the chief normal source of motor impulses for habitual acts and to ascribe their results to vicarious functioning of efferent paths from other cortical areas.

Lashley and Franz (1917) have reported the survival of maze-running and Lashley (1921b) of visual habits after complete removal of the motor areas in the rat. Lashley and Ball (1929) and Ingebritsen (1932) report the survival of more complex maze habits after interruption of the pyramidal paths. Lashley (1924a) found that manipulative habits and habits involving visual discrimination survived the destruction of the precentral gyri in monkeys. From these experiments he has argued that the motor areas are not normally involved in the specific integrations of habits, but are to be regarded as part of the system controlling postural reflexes. Herrick (1926) has criticized this conclusion on the grounds that the experiments are not crucial, but the postulation of a vicarious functioning of some other cerebral mechanism after removal of the precentral gyrus leaves unexplained the immediate production of the complicated patterns of movement which appeared without retraining after the lesions. Lashley (1929a) has found that the habit of traversing a complex maze is disturbed by injuries to any part of the cortex and that equal injuries in different areas have about equal effects. This indicates either a reduplication of specialized paths from lower centers to and from each part of the cortex, without significant transcortical connections or for some reorganization of transcortical activity which involves all parts of the system.

Thus far the attempts to trace conduction pathways involved in habits through the central nervous system have done little more than reveal the difficulty of obtaining evidence either for or against the existence of specifically differentiated conduction paths for learned actions. Most, perhaps all, of the results can be interpreted in terms of reduplication of paths through different parts of the functional areas. On the other hand, the data are equally compatible with an interpretation which denies the existence of pathways specifically differentiated for

the habits through the different functional areas, and this latter interpretation seems more in harmony with the facts of sensory and motor equivalence which will be presented in a later section (see pages 24ff.). The evidence does seem conclusive that the efferent connections of the cortex which control learned or voluntary activity descend directly from the sensory or associative areas without the intervention of the so-called motor cortex.

The mechanism of formation of associations. A survey of recent studies of the conditions under which associations are formed shows that most of the supposed laws of learning from which the nature of the nervous changes involved has been inferred are seriously questioned. Practically all neurological theories of the learning process are based on the belief that the mere repetition of an act tends to fix it as a habit, or that the repeated occurrence together of two stimuli serves to associate them in memory. The older theories have been reviewed by Matthaei (1921) and more recent ones by Lashley (1929b). Starting with the importance of repetition, the theories have postulated the repeated passage of nerve impulses over connecting pathways and a consequent increase in conductivity in these paths brought about by cell growth, changes in intercellular connections, membranes, or the like. Recently Cason (1925) has pointed out that supposed repetition rarely if ever involves an exact or even approximate repetition of the same act. Peterson (1922), Dunlap (1928), and Thorndike (1931) on experimental grounds have denied that repetition in itself is effective in producing learning. Lashley (1929b) has stressed the fact that sensory and motor paths which were not activated during learning may mediate the performance of the habit without additional training.

Such data seem to rule out the formation of associations by the repeated passage of nerve impulses over specific paths, with the concomitant doctrines of local change in synaptic resistance and the like. Alternative psychological conceptions of the learning process are still very vague. Goldstein (1906) and Köhler (1929) have stressed the importance of the organization or Gestaltung of the material and Thorndike (1931) has formulated a similar concept of "togetherness," but so far it is possible to define the effective organization only by the fact of learning, and there seem to be clear exceptions to the rule (Klüver, 1930). The positive inferences concerning possible neurological bases of learning which can be drawn from recent studies are still too vague to permit of any experimental evaluation (Lashley, 1929b).

THE SIGNIFICANCE OF CEREBRAL LOCALIZATION. The association of

diverse cytoarchitectural areas with different functions is well established, but the fact has been emphasized until it obscures the really fundamental problems of cerebral physiology. The production of specific symptoms by restricted cortical lesions furnishes a valuable clue to the nature of cerebral organization but, considered alone, provides no adequate picture of the processes which determine integration. We cannot accept an interactionist theory which localizes psychic entities in the cortical fields and then appeals to psychological laws to explain adaptive behavior. The facts of cerebral localization leave unanswered the question of how the specialized areas carry out their functions and of how their functions are interrelated.

Integration within specialized cortical areas. The character of organization within different cortical fields seems to differ fundamentally. The highest degree of subordinate specialization within single fields has been demonstrated for the stimulable cortex and for the visual area. Especially in primates, stimulation of the precentral gyrus reveals a great number of points whose excitation results in different co-ordinated movements of the skeletal muscles. These have been interpreted by investigators since Fritsch and Hitzig as a mosaic of points directly and more or less exclusively connected with specific motor cells of the cord. Comparison of the position and extent of excitable areas in different animals of the same species and in the two hemispheres of the same animal (Franz, 1915; Stout, 1917; Leyton and Sherrington, 1917) have shown a marked variation which has no obvious counterpart in the behavior of the animals. Lashley (1923) mapped the arm area in the right hemisphere repeatedly at intervals of 1 to 14 days. He found that, although the excitable points remained constant in function (except for the familiar phenomena of facilitation and deviation) during any one period of exploration, there was little correspondence from day to day and the same point might elicit as primary movements entirely different patterns of activity, even movements in different segments of the body. The segmental areas (arm, leg, face) tended to retain a constant position, though with widely varying boundaries, but within each segmental area there was no consistency of primary reactions. From this he concluded that the apparent specificity of excitable points within the secondary areas (head, arm, leg) may be a matter of temporary physiological organization of the area, rather than of stable anatomical connection. Talbert (1900) and Leyton and Sherrington (1917) also report some variability in the effects of stimulation at different times, but less than that found by Lashley.

Experimental studies of differentiation within the visual cortex of animals give far less certain results than clinical studies of man, owing to our lack of any adequate means of mapping scotomas. The older experiments of Munk (1909), Hitzig (1903), and Loeb (1884) seem largely to have missed the projection area and to have interrupted projection fibers or induced temporary trophic disturbances. The experiments of Minkowski (1911) on the visual cortex of the dog are the most decisive available. He finds that the projection areas lie on the posterior and mesial surfaces of the occipital lobe, rather than at Munk's area A. Complete destruction of the posterior half of the field results in permanent homonymous hemianopia in the superior quadrant, of the anterior half a like effect in the inferior quadrant. Any lesser lesions are followed by complete recovery. He interprets the results as showing that each retinal point is projected, not to a single point, but to an extensive area of the cortex, so that only extensive lesions result in the complete destruction of the representation of any point.

Experimental studies of primates have little bearing upon the problem. Munk (1909), Schäfer and Brown (1888), and Panici (1903) found complete blindness only after destructions involving almost the posterior half of the cortex. The recoveries of vision reported by these investigators and by Vitzou (1898), and Franz (1911) did not include the estimation of scotomatous areas and only a limited analysis of visual functions. Recent anatomical studies (Poljak, 1932) indicate that the projection area for the macula in the rhesus monkey, which has been chiefly used in experimental studies, is far more extensive than earlier experimenters have assumed, so that it is probable that considerable portions of the macular area were uninjured in all cases where recovery was observed.

Except for the limited differentiation indicated by Minkowski's studies, experimental work with animals gives no significant evidence concerning the differentiation of function within the visual cortex. We must turn, therefore, to the clinical literature for evidence of functional differentiation within the primary visual cortex. The studies of Marie and Chatelin (1915), Holmes and Lister (1916), Holmes (1918), and Sänger (1918) establish a correspondence between retinal zones and projection fields. The fineness of this differentiation is still in dispute and there is no clear evidence by which we can judge whether there is a distinct point within the area for each ganglion cell of the retina (Henschen, 1917), a pattern of overlapping zones (Minkowski, 1911), or merely a gross polar arrangement with maximal macular effect at the

pole and maximal peripheral effect at the anterior boundary of the area, as suggested by Poppelreuter (1917, pp. 68ff.).

For the somesthetic area the stimulation experiments of Graham Brown (1916) and of Leyton and Sherrington (1917) and the strychnine methods of de Barenne (1916) show differentiation in accord with the receptor surfaces, but details are not established either by the experimental or clinical literature.

In no other cortical area is there any clear evidence of a spatial subdivision with which elementary sensory or psychological units can be correlated. Larionow (1898) and Eliason (Pavlov, 1927) have reported temporary loss of sensitivity to high or low tones following injuries to the auditory areas, but such results have been interpreted by Börnstein (1932) as the result of a general lowering of the level of functional activity and crucial experiments are lacking.

It seems unquestionably established that within some cortical areas, as defined by anatomical methods, there is a subordinate differentiation of function constituting a sort of mosaic. It seems very probable that this mosaic differentiation is not in any case as fine as the peripheral functional units. For other areas it seems equally certain that there is no subordinate spatial representation of functions and that any injury to the area reduces efficiency in a number of activities which are independent in behavior.

It seems significant that the functions for which mosaic specialization within centers is established are just the ones which involve reaction of the organism to the spatial attributes of its environment.

The mechanism of integration within the spatially differentiated centers. In the cortical fields where there is a projection of sensory surfaces, how do the points or foci corresponding to the sensory units function to produce differential reactions? Two opposing views have been advocated, the specialization of each point for a specific reaction, and the functional equivalence of the system. Beyond the tacit assumption that the integration within centers is due to associative connections between neurons, little effort has been made to formulate and to test experimentally hypotheses concerning the functions of a cortical mosaic. Pavlov (1927) has developed a definite theory, making use of the conception of mosaic organization in explaining discrimination of tactile stimuli and of differences in pitch. A conditioned salivary reflex was established to contact on the shoulder and conditioned inhibition to contact on the thigh. Progressive stimulation from shoulder to thigh then resulted in a gradual diminution of secretion with distance from

the shoulder, an indifferent region between the points, and gradually increasing inhibitory effect as the point on the hip was approached. Points in front of the shoulder or on the hind foot produced reactions like but weaker than the trained points. Pavlov interprets this as evidence that separate but adjacent inhibitory and excitatory centers are established in the cutaneous projection area of the cortex from which facilitation or inhibition irradiate so that, as the projected excitation moves across the cortex with change in the locus of cutaneous excitation, the cortical effect shifts from excitation to inhibition. The same hypothesis is applied to discrimination of pitch.

The hypothesis is adequate only for the relatively simplified conditions of his experiments. In the visual discrimination of size we may find a parallel condition. If an animal is trained to choose a white circle of 6 cm. diameter and to avoid one of 4 cm., and is then confronted with a 5 cm. circle there is hesitation, vacillation, with sometimes negative, sometimes positive reactions (neutral zone, Pavlov, 1927, p. 227). A 2 cm. circle and a 10 cm. circle produce some uncertainty of reaction but are definitely negative and positive respectively. The experimental data exactly parallel those of cutaneous or of auditory discrimination. But in this case the circles are fixated successively on the same general regions of the retina and consequently the excitation is projected to the same general areas of the cortex. Further, if the animal is confronted with a 6 cm. and a 10 cm. circle, after successive inspection, he chooses the 10 cm. and avoids the 6 cm. circle. When seen in conjunction with a larger, the previously excitatory stimulus at once becomes inhibitory.

The assumptions concerning a mosaic of inhibitory and excitatory centers is entirely inapplicable to the above data. If we assume a central inhibitory zone surrounded by a circular excitatory zone, the negative reaction to a previously positive stimulus remains unexplained. Further, in unpublished experiments I have found that the animal, trained to choose the largest of three circles may immediately react positively to the widest lines when confronted with three fields with different widths of stripes. There is here no possibility of conformity to preexisting inhibitory or excitatory areas. From what we know of transposition (Köhler, 1929) in audition and discrimination of weights, the mosaic theory is equally inapplicable for these sensory fields, and if it fails here, we must be skeptical of it as applied to the special case of tactile discrimination.

Theory of functional equivalence. Opposed to the mosaic theory of

the functional activity of specialized fields is the concept that within the special area all parts are, in certain respects and for certain functions, equivalent. This view has been expressed by Goltz (1881) with reference to intelligence and the entire cortex, by Lashley (1929a, b) as the equipotentiality of parts, by Bethe (1931) in the theory of "sliding coupling," by Börnstein (1932) and Matthaei (1930) and seems implicit in the systems of Bianchi (1922) and of von Monakow (1914), at least as applied to restricted fields. Three principal lines of evidence have been presented in favor of the theory: the functional equivalence of receptor surfaces, the spontaneous reorganization of motor reactions, and the survival of functions after destruction of any part of nervous centers whose total destruction abolishes them.

The data upon visual discrimination of size presented above are typical of experimental analyses of the sensory determinants in behavior. Becher (1911) formulated the problem clearly in relation to nervous integration. The work of Stone (1922, instincts in rats), Herter (1929), Perkins and Wheeler (1930, visual reactions of fishes), Klüver (1931a, b, visual, auditory, and kinesthetic sensitivity of monkeys), Köhler (1929, chapter V, human vision) and Leeper and Leeper (1932) may be cited as examples of such analysis for different orders of vertebrates. The work shows that, within very wide limits, the absolute properties of the stimulus are relatively unimportant for behavior and the reactions are determined by ratios of excitation which are equally effective when applied to any group of receptor cells within the system (Lashley, 1924b). The significance of these data for interpretation of integration within cortical sensory fields has been discussed by Köhler (1929) and Lashley 1930b).

Experimental studies of spontaneous motor reorganization have been reported by Buddenbrock (1921), Bethe (1931), Lashley (1924a, b), Lashley and McCarthy, (1926), Lashley and Ball (1929). In general the results indicate that when habitually used motor organs are rendered nonfunctional by removal or paralysis, there is an immediate spontaneous use of other motor systems which had not previously been associated with or used in the performance of the activity. In normal human activities an unlimited number of similar instances of transfer can be cited. The shift from writing with finger movements to movements of the arm or even with a pencil held in the teeth still preserves the characteristics of individual chirography. Of course there are limits to such transfer which are set by the fineness and accuracy of the movements involved, but the essential patterns may be imposed upon the muscles of any limb.

Direct experimental evidence on the equivalence of parts of cerebral fields has been presented by Franz (1907), Franz and Lashley (1917), Lashley (1920, 1926, 1929a), Loucks (1931), Maier (1931, 1932), and clinical evidence has been given by Fuchs (1921), Poppelreuter (1917), and Börnstein (1932) among others. The experimental work deals with the formation or postoperative retention of specific habits after the partial destruction of cortical fields. Franz (1907) found that motor habits survived the destruction of the frontal pole of either hemisphere but were abolished by destruction of both. Bianchi (1922) draws a somewhat similar conclusion from his studies with monkeys. Lashley and Franz (1917) found loss of a latch-box habit after complete destruction of the frontal pole in rats, with more or less complete survival of the habit with lesser lesions. In this work there was no adequate control of shock or diaschisis effects. Lashley (1926) found that lesions in the area striata result in a partial loss of habits based on discrimination of light and darkness which is not qualitatively different for different parts of the area, in experiments where shock was controlled by showing that the loss persisted for at least two weeks whereas animals could relearn the habit within the second week after operation. Loucks (1932) found partial loss of the "delayed-alternation habit" after partial destruction of the motor and somesthetic areas which was complete only after very extensive destructions. The significant point in these observations is that a limited lesion does not abolish any identifiable parts of the function, leaving others intact, but lessens efficiency in all aspects of the function.

The same type of result appears after extirpation of parts of the motor cortex of monkeys. Destruction of small areas in general produces only temporary focal disturbances and large amounts must be destroyed in order to produce lasting defects (Graham Brown, 1916; Leyton and Sherrington, 1917).

These three lines of evidence indicate that certain co-ordinated activities, known to be dependent upon definite cortical areas, can be carried out by any part (within undefined limits) of the whole area. Such a condition might arise from the presence of many duplicate reflex pathways through the areas and such an explanation will perhaps account for all of the reported cases of survival of functions after partial destruction of their special areas, but it is inadequate for the facts of sensory and motor equivalence. These facts establish the principle that, once an associated reaction has been established (e.g., a positive reaction to a visual pattern), the same reaction will be elicited by the excitation

of sensory cells which were never stimulated in that way during the course of training. Similarly, motor acts (e.g., opening a latch box), once acquired, may be executed immediately with motor organs which were not associated with the act during training. Bethe (1931) has generalized similar facts under the principle of "sliding coupling" and, following Buddenbrock (1921), has proposed an explanation for motor equivalence based on the assumption that the excitation of a motor center depends upon its tonic state, which in turn is determined by excitations aroused by the state of tension in the motor organs supplied by it. The theory is adequate for the cases of direct adaptation of limb-coördination with which he deals, but seems inadequate for the adaptive reactions described by Lashley (1924b).

QUANTITATIVE RESULTS IN THE STUDY OF CEREBRAL FUNCTIONS. Goltz (1881) first suggested a relationship between the extent of cerebral destruction and the consequent degree of deterioration in more complex adaptive behavior. He interpreted the effect as due to a lowering of attention, implying that the latter is a function of the total energy of nervous activity available. Clinicians have occasionally emphasized the importance of the extent of cerebral involvement in production of general deterioration (von Monakow, 1914; Bianchi, 1922; Head, 1926) but have not presented systematic evidence.

Lashley and Franz raised the question as an experimental problem in 1917 and a number of statistical studies have since been reported. They are summarized in table 1. The use of the correlation coefficient is justified in these studies only as a crude indication of the existence of a relationship. The relationship is probably not rectilinear. Lashley (1926) computed the correlation ratio for lesions in the visual cortex and obtained a value of 0.84 ± 0.03 as compared with a coefficient of 0.72 ± 0.05. From data on 127 cases Lashley and Wiley (1932) find that the retardation is best described as a logarithmic function of the extent of destruction. Beyond establishing that the retardation is disproportionately more severe after large than after small lesions and that the function is a continuous one, the mathematical expression of the relationship has little significance.

The distribution in magnitudes of the coefficients summarized in the table confirms the genuineness of the relationship. Only three of the values available fall between 0.10 and 0.50, whereas five are approximately zero and fourteen above 0.60. This indicates that the functions fall definitely into two types, either completely independent of extent of lesion (within the limits of the tests) or closely dependent. It is not

TABLE 1

The relation between extent of lesion and efficiency of performance in statistical studies of the effects of cerebral injury

The constants are for error scores where these are available, otherwise trials required for learning, or postoperative relearning.

TASK	LOCUS OF LESION	COEFFICIENT OF CORRELATION	REFERENCE
Postoperative retention of simple maze	Frontal areas	Zero	Lashley and Franz (1917)
Learning double platform box	Frontal areas	0.24±0.15	Lashley (1920)
Ibid., corrected for motor disorders		Zero	Lashley (1920)
Initial learning, delayed alternation	Frontal areas	−0.02±0.19	Loucks (1931)
Ibid., postoperative relearning	Frontal areas	0.54±0.12	Loucks (1931)
Postoperative maze learning, 8 culs de sac	Frontal areas	0.64±0.08	Maier (1932a)
Reasoning, postoperative records	Frontal areas	0.54±0.09	Maier (1932a)
Light-darkness discrimination, postoperative learning	Visual cortex	0.08±0.14	Lashley (1926)
Ibid., postoperative relearning	Visual cortex	0.72±0.05	Lashley (1926)
Ibid., corrected for critical area	Visual cortex	0.73±0.08	Lashley (1932)
Ibid., postoperative relearning	Visual cortex	0.64±0.10	Lashley (1930a)
Postoperative learning discrimination two lights	Visual cortex	0.58±0.10	Lashley (1930a)
Postoperative relearning discrimination two lights	Visual cortex	0.65±0.10	Lashley (1930a)
Difference threshold discrimination two lights	Visual cortex	0.49±0.09	Lashley (1930a)
Visual acuity and pattern vision	Visual cortex	All-or-nothing effect	Lashley (1931c)
Reasoning, postoperative records	Visual cortex	0.75±0.05	Maier (1932b)
Postoperative retention reaction to noise	Auditory cortex	0.61±0.11	Wiley (1932)
Postoperative maze learning, 8 culs de sac	All parts	0.86±0.03	Lashley (1929a)

TABLE 1—*Concluded*

TASK	LOCUS OF LESION	COEFFICIENT OF CORRELATION	REFERENCE
Ibid., 3 culs de sac	All parts	0.65±0.07	Lashley (1929a)
Ibid., 1 cul de sac	All parts	0.30±0.16	Lashley (1929a)
Postoperative maze retention 8 culs de sac	All parts	0.51±0.11	Lashley (1929a)
Ibid., 1 cul de sac	All parts	0.00±0.13	Lashley (1929a)
Ibid., 4 culs de sac	All parts	0.80±0.05	Lashley and Wiley (1932)
Ibid., 8 culs de sac	All parts	0.80±0.05	Lashley and Wiley (1932)
Ibid., 12 culs de sac	All parts	0.70±0.07	Lashley and Wiley (1932)
Ibid., 16 culs de sac	All parts	0.60±0.08	Lashley and Wiley (1932)
Ibid., 8 culs de sac reversed	All parts	0.64±0.04	Lashley and Wiley (1932)

possible from the data to formulate any generalizations concerning the activities which fall into these two classes. Apparently the simplest sensory habits and the simplest maze habits show the least relationship to cortical lesion, but the absence of correlation for initial formation of the latch-box and delayed alternation habits does not fit this interpretation on the sole basis of simplicity.

From limited data Lashley (1929a) concluded that in maze learning the deterioration was relatively greater for mazes with many culs de sac. Lashley and Wiley have failed to confirm this, finding that the relative ease of learning simple and complex mazes is the same for normal and for operated animals. In these latter experiments only reduplication of elements in the tests was involved. Where qualitative differences in the tasks are concerned there are indications that small lesions markedly retard some functions such as are involved in the experiments of Cameron (1926), Maier (1932a, b), and Buytendijk (1931), and leave others relatively undisturbed. Jacobsen (1931) found that, after lesions to the frontal lobes in monkeys, the opening of problem boxes with several latches was greatly interfered with although each of the latches alone was opened without difficulty.

The question of what determines relative difficulty of tasks for normal animals and for animals with brain injuries is complicated by many factors. Sensory defects and motor handicaps unquestionably play a

part in retarding the operated animals but in addition to this there are other factors, more clearly indicated in clinical and psychological studies than in the results of physiological experiments. Such conditions as the suitability of the task to the instinctive equipment of the organism, the number of elements which must be dealt with simultaneously in integration, and previous familiarity with these elements, are obviously significant. A number of clinical and psychological studies suggest a still more fundamental factor which cannot as yet be described in terms of the properties of the test situations but only in terms of effects on behavior integration. This is illustrated by the completion of simple figures in the hemianopic field (Fuchs, 1920; Poppelreuter, 1917), by the disturbances of verbal organization in agrammatic aphasia, and in normal psychology by the relative obscurity of different logical relations. Such variations in the difficulty of qualitatively different tasks and indications of specific organizing tendencies in nervous function suggest that the nervous mechanisms tend innately to certain types of integration and that the relative difficulty of tasks is in large measure dependent upon the extent to which they fit this pre-existing schema of organization. The available evidence upon the relation between extent of lesion and difficulty of task is at least suggestive that further investigations may reveal significant correlations.

The fact of a relationship between amount of tissue destroyed and severity of deterioration for certain activities seems firmly established by the data of table 1. Interpretation of the fact still remains in question. Four possible explanations have been suggested, and in part experimentally tested.

1. General shock or metabolic disturbance proportional to the severity of injury. In tests of this it has been shown that some functions which certainly involve the cortex (initial formation of latch-box and light-darkness discrimination habits) are not affected by lesions which produce severe deterioration in other functions (maze learning, "reasoning," various postoperative amnesias). The formation of habits based on light-darkness discrimination is not retarded by destruction of the area striata although injuries in this area markedly reduce performance in Maier's experiments in peripherally blinded animals (1932b). Lesions invading the area striata without destruction of its lateral portions do not interfere with formation of habits based on discrimination of visual patterns, but do retard maze-learning.

2. Deterioration arises from sensory defects due to destruction of the sensory projection areas. To test this Lashley (1929a, 1931a) has compared

the effects on maze performance of destruction of sense organs or sensory tracts with the effects of lesions in the corresponding cortical projection areas. In all cases the deterioration from cortical lesions, which do not completely abolish the sensory functions, is far more severe than that following complete peripheral destruction of sensitivity. Maier has shown that blindness reduces efficiency in his tests but that in blind animals lesions in the visual cortex produce a still greater loss of efficiency.

3. Reduplication of functionally equivalent conducting paths through different parts of the cortex, with deterioration proportional to the number of paths destroyed. This explanation seems applicable to all results on postoperative amnesia except those for the visual area. Lashley (1926) found that linear lesions which interrupted a large part of the optic radiations produced a disturbance only proportionate to the amount of cortical tissue destroyed and not to the extent of interruption of fibers.

It is difficult to see how the hypothesis of reduplicated arcs can be applied to the limitations in learning capacity revealed for mazes and the "reasoning problem." Here we should have to assume that the rate of learning is proportional to the total number of potential pathways available. After destruction of the area striata, or of the posterior half of the cortex, by which the great majority of potential visual pathways have certainly been destroyed the formation of the habit based upon light-darkness discrimination proceeds at normal rate and must therefore be independent of the number of potential cortical pathways. Lashley (1929a) has presented some evidence that retentiveness for habits formed after cerebral injury is reduced and interprets this as meaning that the capacity to retain alterations imposed by learning upon some parts of the nervous system is reduced by the absence of other parts, under conditions where shock or diaschisis are improbable. If this interpretation is correct, it is difficult to harmonize with the maintenance of habits by local alterations of structure. Melton (1931) has suggested that the apparent reduction of retentiveness may have resulted from retroactive inhibition, but this interpretation does not avoid the difficulty for the theory of specific paths.

4. The deterioration is due in part to reduction of some cerebral activity which is not related to specific sensory or motor functions, but is essentially the same for all parts of the cortex. Lashley (1929a) has shown that the loss of the maze habit after destruction of the visual cortex is not dependent upon the sensory function of this area, since the loss is

the same in animals which were blinded by enucleation of the eyes before training in the maze. He also presented some evidence that with lesions restricted to any single cortical area the retardation in maze learning is proportional to the amount of destruction within that area, and that when equal amounts of destruction within different areas are compared, the degree of retardation is equal. Maier (1932a, b) obtained similar results in comparison of the frontal and occipital regions for a different activity. The data of Lashley and Wiley (1932) are less consistent on this point, but support it at least for certain areas.

These facts imply that the activities of any part of the cortex in the acquisition, retention, and performance of more complex integrative functions are conditioned by the activities of all other parts. How this influence is exerted and what its relation to the specific integrative functions of the different areas may be, remains obscure.

NON-SPECIFIC FACILITATION IN CEREBRAL ACTIVITY. Munk (1909) first reported the loss of motility in a limb after section of its dorsal roots with temporary recovery of use during excitement or with restraint of the normal contralateral limb. This type of evidence points to some general facilitative effect of the afferent impulses from the limb, as well as specific reflex integrations. There is a considerable amount of unsystematic evidence that this principle of nonspecific facilitation plays an important part in all nervous activity. The postural system of the cord and medulla, the cerebellum, and the striate complex are generally regarded as not participating directly in the specific integrations of learned activities, but as providing a background of posture and tonus upon which the specific influences of the associative mechanisms are superimposed (Wilson, 1913; Hunt, 1920).

The condition of animals in cerebral paralysis suggests a similar function of the motor areas. Peterson (1931) found that a small injury in the motor area of the forefoot normally used in feeding usually resulted in a shift to the use of the other foot. Injury to the motor area of that foot then resulted in a return to the preferential use of the first. The prompt use of the paralyzed limb in monkeys after amputation of the sound one (Trendelenberg, 1915) and the partial recovery under emotional excitement noted by Minkowski (1917) and Franz suggest that the paralysis is in part due to inadequate facilitation of lower motor centers.

It is uncertain what part such nonspecific facilitative effects may play in cerebral activity. Several lines of evidence suggest fluctuations in some general dynamic condition as important in the production of symp-

toms. Franz has pointed out that the cerebral paralyses in man consist in an enormous difficulty rather than an impossibility of making movements. In the milder amnesic forms of aphasia also there is difficulty in recalling rather than impossibility of recalling verbal material and Head (1926) has noted some of the ways in which the speech mechanism may be facilitated.

A parallel problem appears in the relearning time for habits lost after cerebral lesions. On the first day or two of retraining in light-darkness discrimination the animal with injury to the striate areas makes a purely chance score, irrespective of whether the injury is large or small, or whether the tests follow soon or later after the operation. But with continued training a difference appears. After ten to twenty trials the animal with small lesion begins to make better than chance scores and the proportion of right reactions increases rapidly. The animal with larger lesions continues for a longer time to make chance scores and increases the percentage of right responses more slowly than the other. This corresponds closely to the results of Ebbinghaus (1913) and later psychologists on the strength of the memory trace. In this work it was found that a certain minimal number of repetitions of verbal material are necessary to obtain a correct recall. After a lapse of time recall is impossible but fewer repetitions are necessary to reinstate it. If more repetitions are given than necessary to get recall in the first learning period, fewer will be required for relearning. The longer the intervening time, the more repetitions are necessary to obtain a correct reproduction. This led to the concept of varying strength of associative connections and to the theory that a residual association may exist which is too weak to cause reproduction, but which is effective in reducing the amount of retraining necessary for reproduction. These facts suggest that associations may exist at different energy levels and this seems best expressed in terms of mutual facilitation of the associative mechanisms within the total system of integrations constituting the engram.

The assumption of general dynamic action of the cerebral cortex is common in neurological literature. Upon it depend theories of the release of lower centers from inhibition in explanations of contracture, of hyperesthesias, increased emotional excitability and the like, as well as such general concepts as "vigilance" (Head, 1923), "affective regulation" (Pieron, 1923), and the conception of "dominance" of Orton (1925). The need for critical investigation in this field is obvious.

SUMMARY

The evidence reviewed here can scarcely be regarded as crucial upon any question of the cerebral mechanism of integration, but the picture which it gives us of cerebral activities lacks the precision which was anticipated by earlier workers. There is evidence of mutual dependence of parts in which the specialization of structures seems less important than the mere mass of functional tissue. There are indications that within the entire cortex, for certain functions, and within specialized areas, for others, the subordinate parts are all equally capable of performing the functions of the whole. Even where the highest degree of specialization exists, as in the visual and motor areas, the facts of equivalence of stimuli or equivalence of motor responses preclude any narrowly localized specialization of intercellular connections.

Herrick (1930) has expressed the significance of such data as follows: there is "first, a known localization of stable structural elements whose functions are also known, and, second, a localization of fields within which various recurring patterns of performance or schemata are known to be fabricated and within which inhibition, modification, or conditioning of these patterns takes place." The evidence seems most consistent with the view that these schemata are dependent upon some dynamic patterns of organization such as that proposed by Bethe (1931) for spinal coördination.

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COLOUR VISION

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For the normal person all vision is coloured but for convenience of description one can separate the purely physical aspects of vision from the physiological and psychological problems.

The subject of colour vision is of interest from several points of view, namely:

1. Practical or technical methods, i.e., the methods used for assessing the accuracy of colour discrimination of candidates for the marine, railway and other services.

2. Physiological problems, i.e., the interpretation of facts in terms of the receptors present in the retina.

3. Psychological aspects, i.e., the relation of impulses generated in the optic nerve fibres to the sensations produced.

These three aspects cannot be entirely dissociated in any discussion of colour vision.

In this review an attempt will be made to describe some recent work on colour vision. The reviewer realises that it is impossible to give a complete exposition of the problem of colour vision hence the eclectic plan has been followed. By reference to general articles the reader will be able to pursue the subject further if he so desires.

The plan of the review is an attempt to trace the nature of the receptors present in the retina.

In discussing the subject of colour vision it has been taken for granted that recent experimental work has not lent any support to the view that more than one kind of impulse can pass up the same nerve fibre; in other words, the review is based on the validity of Müller's law.

Edridge-Green (27 p. 263) believes that a single cone can differentiate a series of colours. This differentiation is possible only if different kinds of impulses can be transmitted from the same cone. It is difficult to reconcile this view with the current view of the nerve impulse. (For a general review of the literature on vision up to 1920 see Troland (117).)

PRACTICAL OR TECHNICAL METHODS. There is no fundamental difference between the methods used for the detection of defects in colour vision and those used for the investigation of the nature of the receptors concerned. These methods must be based on stimuli making use of limited regions of the spectrum. The results garnered by accurate examinations of colour discrimination are, however, of importance in relation to the determination of the nature of the visual receptors, therefore they will be discussed later.

For technical purposes measurement of colour discrimination is a problem of importance to those who have to examine candidates for marine and railway services. Such an examination requires a considerable amount of experience and judgment as it is often difficult to draw the line between persons who are liable to make a mistake in circumstances which may lead to serious loss of life and those who can correctly recognise signal lights under all circumstances. It must be pointed out that such conditions as fog, by preferential absorption of light, may alter the quality of a light even for a person with normal colour vision. In view of the fact that well over four per cent of all adult males are colour blind it is unfortunate that traffic signals should be introduced which do not include differences in shape as well as colour.

As the signals to be recognised are always coloured lights it is obvious that the contention of Edridge-Green is correct that the test should always include the recognition of coloured lights.

A Committee of the Medical Research Council is at present considering the methods that can be used for the detection of defective colour vision and until its conclusions have been published it is better not to discuss either the exact form of lantern and other tests that can be used or the procedure to be employed in examining persons for defects in colour vision.

In addition to tests using a spectroscope or coloured lights a wide variety of methods has been used for the technical examination of colour vision. These methods include: sorting coloured wools (Holmgren), classifying coloured beads (127), recognition of letters, numbers or other designs on various backgrounds (126 and 128–132) Bourdier and Schaaff (16) have published a report on the practical application of tests for defective colour vision.

If an individual selects two objects of different colour qualities as being alike the mistake is easily recognised by a person with normal colour vision. By an analysis of the reflection or transmission properties of the two colours it ought to be possible to explain the mistake in terms

of a different appreciation of some part or parts of the spectrum by the person tested, from that by a normal person.

Coloured plates, such as those in which a design is recognised against some sort of background, are constructed so as to cause confusion for those with the usual types of defective colour vision yet to be clearly visible to those with normal colour vision. If such tests are efficient they ought to indicate the kind of mistake which is most frequently made, thus being equivalent to a statistical statement of the common defects in colour vision.

In any test which depends upon the matching of coloured objects their texture should vary, e.g., coloured wools, silks and cottons should be mixed, or transparent and opaque beads should be used in the same test. When using coloured lights their intensities should be varied (see later p. 57 and fig. 1).

PHYSIOLOGICAL PROBLEMS. *Process of stimulation.* The underlying process in vision is photoelectric or photochemical. By this it is meant that light falling on the retina causes an excitation of the atoms which results in chemical change such as the bleaching of visual purple. It has not yet been determined whether more than one photosensitive substance is necessary or if visual purple is actually present in the cones (83, p. 15).

The amount of chemical change produced in a system will depend upon the intensity of the illumination, its duration and the concentration of photosensitive substance; these relationships can be expressed by the equation, $E = k\,I\,t\,c$, in which E is the effect; I, the intensity; t, the duration and c, the concentration.

When screened from light the retina becomes more sensitive. This change can be explained by the reformation of photosensitive substance either from its products of decomposition or from other sources.

Stimulation of the visual receptors is presumed to be brought about either directly or indirectly by products of photochemical decomposition, but, as in all methods of stimulation of receptors or nerves, a minimal amount or threshold value is necessary. From a purely photochemical point of view stimulation of the receptors should continue until the quantity of stimulating material has fallen to threshold value. The occurrence of after-images indicates that the process does continue after the light stimuli have been cut off, but the continuance of the sensation depends upon other factors such as subsequent stimulation by light (see p. 73).

The observed facts of an animal's response to stimulation by light are

in favour of an explanation based on the kinetics of a photochemical reaction outlined above. Hecht (45, 46, 49, 52, 53 and 55) has studied the latent period between the exposure to light and the subsequent response with Mya arenaria, Pholas dactylus and Ciona intestinalis. He found that the length of the latent period depends upon the product of intensity of illumination and its duration. Adrian and Matthews (5) have found a similar relation between the quantity of light and the duration of the reaction time for the eel's eye.

There are obvious complications to such a simple view as that described above. The quantity of photochemical products must be above the threshold value and the threshold itself may vary with the condition of the nerve endings. The area of the retina stimulated has some inverse relationship to the intensity of light required to produce a sensation.

Adaptation. Alteration in the sensitivity of the retina can be due to change in the amount of photosensitive substance. By excluding light the sensitivity of the retina increases and the amount of visual purple accumulates. Exposure to light, by bleaching the visual purple, reduces the sensitivity to light. Tansley (114) has studied the regeneration of visual purple in rats. The animals, after being exposed to bright light were transferred to a dark room. At definite time intervals animals were killed and the visual purple extracted by digitonin. Curves showing the rate at which visual purple regenerated correspond to either a monomolecular or bimolecular reaction. Hecht (51, 52) in Mya and Ciona found that the time relation of increase in sensitivity agreed with what would be expected from a bimolecular reaction. In other words, it seemed as if the photosensitive substance was regenerated from two precursors. Hecht (47, 48) found a similar relation for the increase in sensitivity of the human eye during dark adaptation.

If by adaptation we mean the increase in the amount of photosensitive material during dark adaptation there are other processes to be considered. Variation in area of aperture of the pupil is a purely physical method of regulating the intensity of light which reaches the retina. There is also the process of induction whereby the sensation may be altered by illumination on another part of either the ipsi- or contralateral retina. Induction may be due to summation, occlusion, or inhibition, at some of the synapses in the path of the visual impulses. Roaf (96, 98, 102, 103) has investigated the effect of coloured lights in altering the threshold when the lights shone on the same and on other parts of the retina. Lythgoe and Tansley (76) have examined the critical frequency of flicker on different regions of the retina and at various

stages of adaptation. Granit and von Ammon (37) have observed the change in frequency at which flicker disappears during exposures of six seconds. Lythgoe (75) has recorded the changes in the recognition of colours on the peripheral retina during dark adaptation.

Gelhorn (31) has studied the effect of fatigue on the extent of the fields for colour. Gelhorn and Fabian (32) have shewn that direct exposure to the same colour, by diminishing the colour value decreases the differential threshold for light intensity but that preëxposure to a complementary colour increases the differential threshold. Preëxposure of the contra-lateral eye raises the threshold both for the same and complementary colours. Vogelsang (119, 120) finds that the sensitivity and reaction time of the eye are increased during dark adaptation.

Most of the above authors were measuring the effect of time intervals on the progress of adaptation and their results are not related to the interpretation of the kinds of receptors present in the retina. Talenti (112) found that there were no specific differences between the colours. Lythgoe and Tansley (76) state that "red" stimulates cones only and gives only one type of flicker curve. They also conclude that the extra foveal cones are not functionally identical with foveal cones. Lythgoe's observations on extra foveal colour vision will be referred to later (p. 69).

A study of the process of stimulation and that of adaptation to light is essential if one is to solve the problem of colour vision. The relation of coloured light to receptors in the retina is dependent upon the photosensitive substance or substances in them. Edridge-Green (27 p. 9, 28) goes so far as to state that the rods have no function other than the preparation of visual purple and that the chemical substances produced by bleaching the rhodopsin stimulate the cones. It is unfortunate, so far as a knowledge of the mechanism of colour vision is concerned, that so many workers do not use light from a restricted region of the spectrum. "White" light produces complicated results which are very difficult to interpret.

Nature of receptors. We cannot decide about the underlying physicochemical processes which produce stimulation until we know what receptors are present in the retina. Indeed this problem is often considered to cover the whole subject of colour vision.

There seems little doubt that the simplest basis for colour sensations is the hypothesis of Young (125) that "it becomes necessary to suppose the number limited to three principle colours." This view is based on the physical facts that all colours can be reproduced by combinations of three suitably chosen regions of the spectrum. It is true that white light

may be necessary to dilute the colour which is being matched but as white light can be reproduced by the same three colours the coördinates merely need correction for the components added in the white light. Wright (124) has made accurate determinations of the "red", "green" and "blue" values for the different parts of the spectrum. The general application of Young's hypothesis as developed by Helmholtz has been discussed recently by Hecht (56), Parsons (84) and Piéron (87).

If more than three receptors are shewn to be present or if experimental observations require more than three receptors then the theory must be more complicated but at present such an extension is not necessary.

As all colours can be reproduced from three homogeneous bands of the spectrum, normal vision can be said to be trichromatic. If a defect in colour vision occurs so that all colours can be matched by two bands from the spectrum the vision can be said to be dichromatic. Similarly if there is no distinction of one colour from another, except by differences in intensity the vision is said to be monochromatic. As persons with defects in colour vision usually distinguish fewer colours than normal individuals they can be described as hypochromats and their condition spoken of as hypochromatopsia.

Edridge-Green (27) uses a different nomenclature depending on the number of colours that the person can name in the spectrum. The normal person recognises six (occasionally seven) colours hence they are called hexachromics. Those who recognise five, four, three, two and one distinct colours he calls penta-, tetra-, tri-, di- and mono-chromics respectively. Edridge-Green's nomenclature is good in so far as it merely describes the condition of the person's vision but it is difficult to be certain whether the colours said to be seen are correctly discriminated. It is, however, confusing because a person who recognizes three colours in the spectrum, a trichromic, is not the same as a trichromat for whom all colours can be constructed from three spectral regions. A similar confusion occurs with the terms dichromic and dichromat. One point to which his nomenclature does call attention is that there are varying degrees of defective colour vision.

Colour or wave length discrimination. One method of studying colour vision is to measure the threshold for colour discrimination. This method consists in comparing two regions of the spectrum and recording the least difference in wave length that will give rise to a recognisable difference in colour. Steindler (111), Jones (63a), Laurens and Hamilton (74) and Roaf (97) all agree in showing two main maxima of discrimi-

nation, one in the "yellow"[1] and the other in the "blue-green." Steindler, Jones and Laurens and Hamilton found subsidiary maxima but with reference to one of these the latter authors state (42, p. 576) "The orange minimum is frequently absent in normal curves." The minimum referred to is a minimal difference in wave length which corresponds to a maximum of discrimination. Edridge-Green has mapped out the

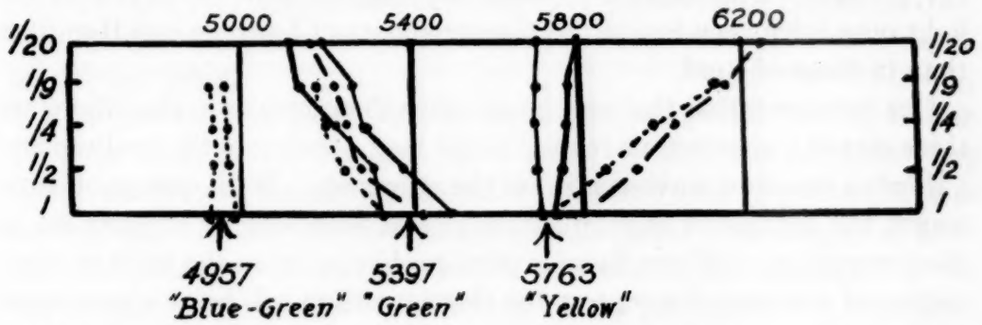

Fig. 1. Effect of decrease in intensity on the colour discrimination of an euchromat and a hypochromat. Ordinates show the reduction of the fixed wave lengths to $\frac{1}{2}$, $\frac{1}{4}$, $\frac{1}{9}$ and $\frac{1}{20}$ of their original intensities. Abscissae show wave lengths of the spectral lights, each division corresponding to 400 Å. The experimental points show the wave lengths of the lights which just appear different from the fixed wave lengths 4952, 5397 and 5763 Å respectively, indicated by the arrows. For the euchromat (points joined by continuous lines): note that with "yellow" the lines are close together and do not show any shift with decrease in intensity, whilst with the "green" the lines are further apart and with decrease in intensity of the fixed wave length it is matched with a colour more towards the "blue" end of the spectrum. For both the hypochromat and the euchromat the results with "blue green" coincide (points joined by dotted lines). The lines are close together and do not show any shift with decrease in intensity. For the hypochromat with "yellow" and "green" fixed lights the range of discrimination is identical and it becomes wider with decrease in the intensity. In order to show these curves the points for the "yellow" fixed light are joined by dotted lines whilst those for "green" are indicated by a single dash between each pair of experimental points. These curves show quite clearly that this hypochromat made no distinction between "yellow" and "green" as the wave lengths that just appeared different are practically identical for the two fixed lights. Redrawn from the data of figure 4, Quart. Journ. Exper. Physiol., 1927, xvi, 387.

spectrum into monochromatic areas (27 p. 177) and he found that these were narrower in the "yellow" and "blue-green."

Roaf's measurements were more concerned with the problem of how differences in intensity between the two lights which were being com-

[1] The terms "red," "yellow," etc., will be used to denote light of such wave lengths as would give rise to the corresponding sensation for a normal individual.

pared would influence the accuracy of the discrimination, especially of those with defective colour vision (see fig. 1) hence the secondary maxima were neglected. The range of wave length necessary for discrimination was greater in the measurements of Roaf than in those of Steindler, of Jones and of Laurens and Hamilton but they are more in agreement with the method of Edridge-Green in measuring monochromatic patches (27, p. 185). Unpublished experiments suggest that the purity of the light may have been less in the measurements of Laurens and Hamilton than in those of Roaf.

One interpretation that can be given to these results is that there are three sets of receptors, one related to the long, another to the medium and a third to the short wave lengths of the spectrum. With change of wave length the maximum of stimulation passes from one to another set of these receptors. Where there is most rapid change in the ratio of stimulation of two sets of receptors the discrimination will be at a maximum hence "yellow" can be looked upon as the region of sharpest transition between stimulation of the receptors for long and medium wave lengths. Likewise "blue-green" may be regarded as the region of sharpest transition between receptors for medium and short wave lengths.

Taking for granted that the above observations indicate that there are three kinds of receptors with a rapid alteration in their relative stimulation at the "yellow" and "blue-green," we can attempt to find out to what extent the stimulation is confined to definite regions of the spectrum and to what degree the receptors overlap.

Hamilton and Laurens (42) compared the discrimination for normal individuals after exposure to bright spectral lights. They found that after exposure to "red" the maximum in the "yellow" was absent whilst after exposure to "green" the discrimination was less affected than after "red" but the maximum of discrimination in the "yellow" was also absent. After exposure to "blue" the maximum in the "blue-green" was greatly diminished. Other regions of the spectrum did not produce clear cut effects.

Troland (115) measured the effect of previous exposure to bright lights and he found that "minuthesis due to one colour does not alter the luminosity of another colour to a degree differing appreciably from that in which it is altered itself." The term minuthesis was used to indicate decrease in the sensation brought about by previous stimulation. His results indicate that there is no specific effect of wave length on the brightness of a succeeding sensation provided that the original stimuli had been of equal brightness.

The effect of simultaneous exposure to two regions of the spectrum has been systematically studied by Roaf (96, 98, 103). The threshold of a test light was measured and then the increase in that intensity necessary for the light to be visible on some illuminated background. The background was always from a limited region of the spectrum, therefore the observations differ from those of Cobb (21), Cobb and Geissler (22), Lythgoe (75), Lythgoe and Tansley (76, 77), Priest and Brickwede (89) and Talenti and Meineri (113) who used heterochromatic or "white" modifying lights.

Roaf's work was based on the hypothesis, founded on the Weber-Fechner Law, that if the two lights acted on different receptors they would not greatly interfere with each other but if they acted on the same endings more or less interference would take place. The degree of overlap in stimulation by two lights would be shewn by the change in threshold of the test light due to bleaching of the photosensitive substance. Changes due to induction (i.e., the effect of simultaneous exposure of other parts of the retina to light) must be distinguished from those due to adaptation (or bleaching of visual purple) by comparing the changes in threshold when the eye is simultaneously illuminated on the same or some other part of the retina. The test light is always the one of which the threshold value is being measured whilst that light which is producing a change in threshold is known as the modifying light. The modifying light is sometimes used as a surround and sometimes as a background to the test light. The results are illustrated in figure 2.

For foveal vision it was found that a "red" modifying light raised the threshold for all parts of the spectrum, in fact the thresholds of the "green" and "blue" test lights were raised to a greater extent than that of the "red" test light. This result suggests that the long wave length end of the spectrum stimulates receptors for all the other parts of the spectrum thus raising the differential threshold[2] for all lights.

A "green" modifying light has comparatively little effect in raising the threshold for "red", this suggests that the receptors for the long wave length end of the spectrum are only slightly affected by medium wave lengths but "green" raises the thresholds for both "green" and "blue" to a considerable degree.

[2] The amount of extra light which must be added to a fixed light in order to produce a just perceptible difference in brightness is known as the differential threshold. The absolute threshold is the intensity of the least amount of light which is visible when no other light is present and the eye is in a condition of dark adaptation. If both these thresholds are measured the differential threshold can be expressed as the multiple of the intensity of the absolute threshold.

A "blue" modifying light like the "green" one raises the threshold for "red" to only a slight extent, it has more effect on the threshold for "green" but most on that for "blue."

These results suggest a new point of view on the nature of the receptors, namely, that the long wave length end of the spectrum stimulates

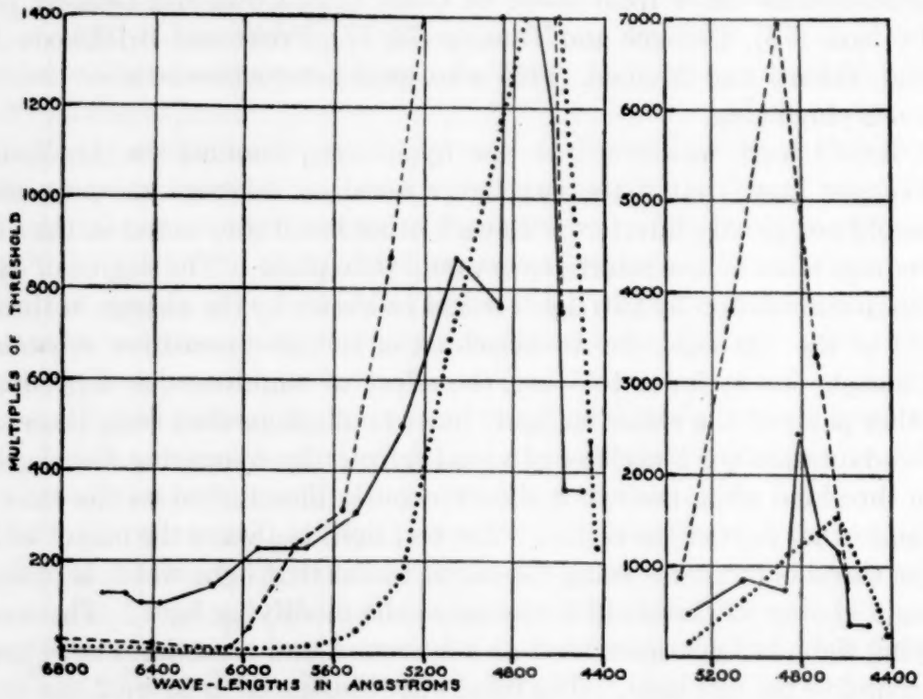

Fig. 2. Ordinates, multiples of the absolute threshold; abscissae, wave lengths in Å. In order to show the higher values a part of the range is reproduced in one-fifth of the scale. Continuous line shows the effect of a background of 6214 Å in raising the thresholds. Interrupted line shows the effect of a background of 5404 Å and the dotted line the influence of a background of 4708 Å. Note the marked effect of all the backgrounds in raising the threshold for the shorter wave lengths whilst the "green" and "blue" backgrounds do not raise the threshold for "red" to anything like the same degree as the "red" background does. The long wave length portions of the curves are horizontal agreeing with the conclusion that the "red" differs only in intensity but not in quality. (Reproduced from Nature, 1930, cxxvi, p. 825.)

all the receptors in the retina whilst the shorter wave lengths stimulate only some of them. In the experiments the "red" was sharply demarcated from the rest but there was much greater similarity between the "green" and "blue." This point of view will be discussed under the heading of interpretation of results. The results for extra foveal vision will be mentioned later (see p. 69).

In view of the similarity observed between the results with "green" and "blue" it is interesting that the short wave length end of the spectrum can be demarcated from the rest by its lower acuity of vision. König (67) found that the ability of the eye to discriminate differences of detail differs from the resolving power of an optical instrument in that it depends on the brightness of the illumination. He noticed that the visual acuity with "blue" light was very poor but ascribed the lack of recognition of detail to weakness of the light.

Roaf (101) has reëxamined this problem from the point of view that the difference between "blue" and the rest of the spectrum depends on some physiological difference in the nature of the receptors. He measured the legibility of transparencies, with opaque letters of different sizes, against a background of coloured light. He, likewise, found poor acuity with "blue" light and he pointed out that if the result were due to insufficient brightness it was still of significance. Thus if physically equal multiples of the intensities which correspond to the absolute thresholds for each colour are compared the "blue" light is much inferior to the others for the appreciation of detail.

The discussion of this problem is bound up with that of heterochromatid photometry. It is possible to compare two lights of different colour in various ways. Equal energy values of radiation are not physiologically equal, but physiological comparisons can be made by the "equality of brightness" method, by the "flicker" photometer or by measuring the threshold to light. These methods can be used to compare lights of different wave length but unfortunately measurements given in candle power or millilamberts are often deceptive. For instance, the brightness of the light has been measured against a standard heterochromatic ("white") light but the author (e.g., 22) does not state whether the comparison has been made at the intensity used for the experiment. Owing to the Purkinje effect, namely, that the brightness of a light of long wave length increases more rapidly for a given multiple of its intensity than does one of short wave length, comparisons made at one intensity are not valid at another (83, p. 63).

Thus we see that if poor acuity in "blue" light is due to insufficient brightness of that light we are dealing with a physiological rather than a physical property of the light. Physically the resolving power of an optical system is greater for "blue" than for longer wave lengths.

If two lights of different wave length are considered as being of equal physiological value at their threshold and if they are both increased until their energy value is x times their value at the absolute threshold then

as they are no longer of equal brightness as judged by the "equality of brightness" or "flicker" methods, there is some difference in the ratio of brightness to energy value (61). It seems legitimate to conclude that this difference in ratio is most easily explained by a difference in the nature of the physiological receptors.

A significant point is that the decrease in visual acuity occurs sharply on the "blue" side of the "blue-green" where there was found to be a maximum of wave length discrimination.

Allen and his co-workers (8–13) have studied the influence of various modifying lights on the duration of interruption at which flicker disappears. The results are rather difficult to summarise but the main conclusions are: Light shining on one part of the retina, depending upon its intensity, may either increase or decrease the sensitivity of the ipsi- or contra-lateral retina.

There are certain equilibrium colours which do not influence the interval at which flicker disappears.

The Weber-Fechner law holds over only narrow variations of intensity. With wide variations in intensity the curves show breaks so that they consist of a series of straight lines each with a different constant.

The interpretation, given by Allen, that the results measure the sensitivity of the eye to light requires some consideration. Sensitivity of the eye increases during dark adaptation yet Allen finds that under some conditions the sensitivity is increased by illumination. This difference may be due to the fact that for dark adaptation the sensitivity is measured by the intensity that will just stimulate whilst the duration at which flicker disappears is measured at a much higher intensity.

This section shows that there is a prima facie case for the view that there are three groups of receptors. The first (that associated with "red") is differentiated by the fact that its threshold is only slightly raised by lights from other parts of the spectrum. The third (that associated with "blue") is characterised by the poor acuity of vision in light of short wave length. The second is differentiated by its poor effect in raising the threshold of the first and by its superior effect, to that of the third, on visual acuity. The transitions from the region where one of these predominates to that of the sphere of influence of the next are probably most rapid at the maxima of discrimination in the "yellow" and the "blue-green."

Congenital defects in colour recognition or red-green confusion. Defects in colour recognition should be related to the kinds of receptors present in the retina. The literature on this subject is voluminous and can be

found in standard books of reference (71, 83, 92). One difficulty is that in the past names have been employed for the different kinds of defect which depend upon some theory of colour discrimination. The terms protanope and deuteranope would have been unobjectionable if they were not usually understood to be synonymous with "red blindness" and "green blindness" respectively and to imply that red and green are not seen. It would be much better if cases were described according to the observations made on them. Thus the term red blindness should be used only when there is a decreased sensitivity to the long wave length end of the spectrum (18) as blindness implies insensitivity to light.

The usual type of defect is a failure to discriminate between red and green which is not always accompanied by any decreased sensitivity to light (i.e., the achromatic threshold is not raised and the spectrum is not shortened (17, 83 p. 184)). As there seem to be all degrees of defect the results of examination of cases are variable but the region between "red" and "green" is always affected and yellowish shades in particular are confused (see fig. 1).

In view of the fact that decreased sensitivity to light does not always occur it is preferable to speak of red-green confusion rather than red or green blindness. Confusion describes the condition, namely, a failure to distinguish some part of the spectrum from another (18).

The complete failure of discrimination giving rise to monochromatic vision or what is called complete colour blindness is very rare and will not be described.

Steindler (111), Laurens and Hamilton (74) and Roaf (97) have examined the colour discrimination by means of a spectroscope. Steindler (111) found a maximum of discrimination at about 5030 Å for five deuteranopes and two maxima at about 5000 and 5980 Å respectively for three protanopes.

Laurens and Hamilton (74) found for one protanope that the maximum of discrimination which Steindler found to be present about 5980 Å (i.e., in the "yellow") is absent. They point out that the second maximum found by Steindler may have been due to differences in brightness. Roaf (97) has examined a number of cases of defective colour vision and finds that invariably they fail to show the maximum of discrimination in the "yellow." Edridge-Green by his method of measuring monochromatic patches finds that the patches are wider in the "yellow" for hypochromats than for normals. Houston (63) by measuring the number of steps of just recognisable differences between three selected colour screens found that the colour triangles constructed

from his results were deformed. Examination of Houston's figures show that the deformity was mostly due to fewer steps between the "red" and "green."

All these results show that the usual colour defect is a failure to discriminate in the interval between the long and medium wave length region of the spectrum.

A simple method of showing the usual type of colour defect is to obtain copies of coloured diagrams made by hypochromats and to examine these to find out which region of the spectrum is seen differently from what it appears to the normal person. An old fashioned device (105 p. 98, 123 p. 115) was to examine paintings, made by hypochromats, through coloured media but Roaf (94) has applied the method of examining the original and copy in the light of a recombined spectrum from which any portion can be excluded. It is best to make the paintings with highly unsaturated colours so that there is a large amount of nonspecific light (white) reflected from the coloured patches. If such paintings are examined and different parts of the spectrum excluded from the recombined light it will be found that the difference between the copy and original will disappear if one allows for the change in intensity, due to differences in reflection by the colours, of that portion of the spectrum which has been excluded. The difference will disappear only if the "red" end of the spectrum is excluded. Over 40 cases have been examined by this method (some still unpublished) and although the amount of spectrum removed varied the "red" must always be excluded. None of these cases could be classed as green blind because none of the diagrams matched by exclusion of only the middle of the spectrum. Nor could they all be classed as red blind as in some cases there was no decreased sensitivity to the long wave length end of the spectrum. These results like the preceding ones on colour discrimination point to a failure to distinguish the long wave length end of the spectrum in the same way that it is discriminated by a normal person.

Thus we see that any explanation of colour vision in terms of receptors must allow for the disappearance (partial or complete) of the power of distinguishing the long wave length end of the spectrum from the rest without necessarily a loss of sensitivity to light.

It is also recognised that there are two main divisions of red-green confusion (83 p. 192) but the nature of the difference is not yet understood. One type shows no decreased sensitivity to light whilst the other seems to have decreased sensitivity to "red" and perhaps to other parts of the spectrum.

It is very difficult to obtain accurate measurements on untrained subjects, as all sorts of adventitious aids are used, either consciously or unconsciously, to help in the recognition of colour. This problem is more correctly one of psychology but it must be mentioned here. Differences in shape or position suggest the nature of an object, hence its colour. At sea two lights seen close together would be expected to be the right one, red and the left one, green. Such obvious aids can be easily excluded but the influence of intensity differences must also be excluded in testing for defective colour vision. A striking example of the influence of intensity is when a hypochromat declares that the colour has been changed from yellow to green when all that was done was to reduce the intensity of spectral "yellow." As the brightness values of lights may differ for normal persons and for those with defective colour perception, lights which to the euchromat may appear of equal brightness may appear of unequal brightness to an hypochromat. Therefore the intensity of the same light should be altered during an examination to see if that will confuse the examinee. This factor of brightness was varied by Roaf (97) and he found that some hypochromats who showed (at times) good discrimination in the "yellow" were completely confused when the intensities were unequal. Persons with normal colour vision show differences in matching spectral colours if the intensities are different but these changes occur only where discrimination is at a minimum that is, in the "red," "green" and "blue." In the "yellow" and "blue-green" differences in intensity make no alteration in colour matching for the normal person (see fig. 1).

The most hopeful method of classification is to consider the two classes as being extreme degrees of anomalous trichromatism (118). Rayleigh (91) found that there were two classes of individuals without any obvious defect in colour vision; distinguished by the relative proportion of "red" (lithium line 6708Å) and "green" (thallium line 5351 Å) to match a homogeneous "yellow" (sodium line 5896Å). This difference in relative proportions is seen in the measurements of Abney (2, p. 276) and Watson (4, 121). The latter showed by the "flicker" method that the relative luminosity of "red" and "green" was not the same in all individuals. The problem of anomalous trichromatism will be referred to under the heading of interpretation (see p. 70).

The various practical tests for the detection of defective colour vision usually distinguish between "red blind" and "green blind" or protanope and deuteranope according to the classification preferred by the author. Examination of some of these tests, for example that of Ishihara, is

of interest as their composition illustrates the usual mistakes made by hypochromats.

Each of Ishihara's plates (128) consists of a series of discs of different sizes on which the colours are printed with different degrees of saturation. Owing to this difference in size and saturation the only criterion for recognising the design is the difference in hue. The main device is to have orange vermillion numbers on a yellow green background (or vice versa) which the hypochromat fails to read because he fails to distinguish the red from the green tint. By the introduction of blue the vermillion becomes carmine or mauve and the green, blue green. A hypochromat recognises the blue and distinguishes carmine from vermillion and blue green from green. Thus by constellations of the four colours, plates can be produced with numbers that can be read by euchromats because the reds (vermillion and carmine) are distinguished from the greens (yellow green and blue green). In the same figure a different number will be read by hypochromats as they group together vermillion with yellow green and carmine with blue green.

For example, plate 2 (128) shows, for the normal person, the number 8 in carmine and vermillion on a green background. The hypochromat fails to distinguish the vermillion near the right side of the cross piece of the 8 from the green background. Hence he sees the number 3, the turned in ends of which are completed by some blue green spots which appear like the carmine and different from the green background.

To return to the two groups shewn by such tests. Figures 12 and 13 of Ishihara (128) and figures 9 and 10 of Schaaff (130) all distinguish the two classes because the one class ("red blind") cannot read vermillion objects on a grey or grey brown background but they can distinguish mauve or carmine on the same backgrounds whilst with the other class ("green blind") the conditions are reversed. Vermillion reflects predominately the "red" end of the spectrum whilst carmine and mauve reflect both ends more than the middle. Therefore all these colours reflect less of the middle ("green") and it looks as if the distinction was based more on the amount of short wave length light reflected than on the absence of "green." Figures 7 and 8 of Schaaff are more difficult to explain. In figure 7 neither of the colours reflects much "blue" but in figure 8 the blue-green background reflects more "blue" than the grey design.

In all the charts it is clear that the defect is always a failure to distinguish red (e.g., orange vermillion confused with yellow-green and carmine with blue-green) the difference is that some other additional

factor is concerned which may be the position of the neutral band in the spectrum. To say that the failure to recognise crimson is due to "green blindness" is rather confusing as vermillion is seen as different from the background and it, like crimson, reflects little of the mid region of the spectrum. It may be that something more positive is involved, namely, the blue element in the crimson which is absent from the vermillion. It is true that the light and shade effect between the design and its background must be a factor in the recognition of the object. Owing to the outstanding effect of "red" for the euchromat the light and shade difference is difficult to assess.

In order to distinguish the two classes of hypochromat Rivers (92, p. 1091) introduced the terms photerythrous and scoterythrous indicating that some are as sensitive to "red" as euchromats whilst the others are relatively less sensitive. In the description of many cases the statement is made that the "red" end of the spectrum is shortened but unfortunately no reference is made to the sensitivity to light from the rest of the spectrum. Akesson (7), for instance, has measured the relative insensitivity of a protanope only at the "red" end of the spectrum but Bradbrooke and Roaf (17) found that there was decreased sensitivity for all parts of the spectrum examined. Raehlmann (90) found that the "blue" end of the spectrum was shortened in some cases.

The colour vision of all these well marked cases of red-green confusion can be reproduced using two bands from the spectrum, one on each side of the "blue green;" they are therefore instances of dichromatism.

Von Kries and Nagel (72) measured the amounts of "red" and "blue" (4608 Å) to match the various parts of the spectrum. They found very little difference in the intensity of "blue" required for matching by both protanopes and deuteranopes. They stated that the proportion of "red" required in the various matches differed for protanopes and deuteranopes but the curves cannot be directly compared because the "red" used for protanopes was really a "yellow" (5892 Å) whilst that for dueteranopes was a true "red" (6450 Å). This choice was made because of the low luminosity of the long wave length end of the spectrum for protanopes.

Thus we need to know the colour discrimination, the presence and position of any neutral band in the spectrum, the sensitivity to light throughout the spectrum and the relation of brightness to intensity in different spectral regions, in a series of hypochromats.

Blue blindness. Another type of defect in colour perception is known as blue blindness or tritanopia. This defect, like red-green confusion, is

a form of dichromatism in which two colours from the spectrum will suffice to reproduce all colours. In this case "red" and "green" are the two colours that can be distinguished. There is a definite decrease in sensitivity to light especially that from the "blue" end of the spectrum (65), (83 p. 191). There is a neutral band in the "yellow green" (about 5700 Å). This form of defect is quite easily explained on the basis of the Young-Helmholtz hypothesis on the supposition that the receptors for "blue" are absent. Although of considerable theoretical importance it is negligible for technical purposes. Collins (23) and Deiter (24) have each described a case of blue blindness.

Other varieties of defective colour perception exist such as tobacco amblyopia and those due to cerebral lesions but it is not necessary to discuss them here. Nor need we consider cases of uni-ocular colour confusion, which are all fully described by Köllner (65).

Interpretation The explanation of colour discrimination offered by Helmholtz' modification of Young's hypothesis cannot be reconciled with the facts, otherwise we would not find so many attempts to alter it. On the other hand the evidence presented in the preceding section is in favour of there being three types of receptors with a maximum ratio of changes of stimulation at about the "yellow" (5800 Å) and the "blue-green" (4900 Å).

The chief alternative theory is that of Hering (61), namely, that there are three photosensitive substances each of which is decomposed by light of a certain particular wave length and recombined by the corresponding complementary colour. This hypothesis is founded on a psychological basis and expresses many relationships particularly with reference to contrast effects, but it is improbable from the photochemical point of view. Even the ingenious modifications of Ladd-Franklin (60 pp. 464–468), that "red" splits off one substance and "green" another and that combination of these two substances gives rise to a sensation of yellow whilst "yellow" light causes a splitting off of both these substances with their combination to give the sensation of yellow, cannot overcome the objections to the theory.

One insuperable objection to the Hering hypothesis is that put forward by MacDougall (78) on the basis of binocular combination of colours. If a suitable red field is presented to one eye and a green field to the other, in the absence of rivalry or a markedly "master" eye, a sensation of yellow is produced. This binocular combination proves that the yellow sensation can be produced in the cerebrum as the result of impulses which would cause the sensation of red and of green when each

was presented separately. Therefore no process whereby a red-green substance can be kept in equilibrium by balanced "red" and "green" stimuli whilst the yellow-blue substance is decomposed by both coloured lights, will account for binocular combination. The same objection to Hering's hypothesis was given by Roaf (98, p. 246) who used spectral lights. Hecht (54) has constructed a simple apparatus by which this combination can be demonstrated. It was in view of the insuperable objection to Hering's hypothesis that the data in the preceding section were marshalled to show the probability of three separate receptors.

Helmholtz' hypothesis presents difficulties especially in relation to red-green confusion. If for instance the red perceiving mechanism were absent there would be a considerable shortening of the long wave length end of the spectrum. An attempt has been made to avoid the necessity for a decrease in sensitivity to "red" by suggesting that the receptor for the middle of the spectrum alters its photosensitivity to compensate for the loss of the receptors for "red" (3, 118). It is unlikely that a photosensitive substance would alter its sensitivity to light in such a convenient manner. If the sensation curves given by various exponents of the Helmholtz hypothesis were correct it would be difficult to explain the marked influence of "red" in raising the threshold to "blue" described in the previous section (see fig. 2).

Hecht (56, 57, 58) has recently made an ingenious reshuffling of the data for colour mixing, luminosity of the spectrum, etc. He points out that the facts of colour mixing can be explained on the basis of a combination of three separate regions of the spectrum but that these regions can be selected to correspond to a wide variety of photosensitive substances. He has recalculated the data from various sources and states that the results can be explained on the basis that there are receptors present each of which contains one of three photosensitive substances. The curves showing the wave lengths to which these substances are sensitive lie very close together. Hecht (58) shows these curves. Such curves indicate that they[3] would appear like visual purple and it would be very difficult to show separate substances with such closely allied absorption curves. Hecht's papers are of interest as they show how greatly one can vary the sensitivity curves of the supposed receptors from those suggested by Helmholtz and others whilst retaining them to explain the facts of colour mixing. Hecht (58,

[3] Hecht speaks of these curves as indicating the absorption of light but although this statement is probably correct it does not necessarily follow that the chemical action is directly proportional to the amount of light absorbed.

p. 82) points out that the difference between the two common forms of hypochromatopsia still requires some further explanation. In view of Hecht's adequate statement of his hypothesis it is not necessary to describe it here, in detail.

The objections to Hecht's curves for the photosensitive substances are:

1. It seems unlikely that curves of such similar photosensitivity would differentiate colour stimuli to a sufficient degree.

2. The curves would not explain the effect of a "red" background in increasing the threshold to "blue" whilst a "blue" background has so little effect on the threshold for "red".

3. It is difficult to see how one can explain the poor acuity in "blue" light with curves of such similar photosensitivity.

Another departure from the classical Helmholtz modification of Young's hypothesis is that advocated by Roaf (96, 98, 100, 103) on the basis of experimental work described in the previous section. The fundamental points are that "red" stimulates all the receptors in the retina, "green" stimulates two and "blue" or "violet" only one.[4]

To explain this relationship we can assume three sets of receptors one sensitive to the whole extent of the spectrum (c), one sensitive to a region extending from the extreme "red" end to about 4900 Å (b), and one sensitive to the "red" end only up to about 5900 Å (a).

As "red" light would stimulate all three of these we can see how light from that region of the spectrum would raise the threshold to the whole spectrum. At the same time the sensation of red must be accompanied by inhibition of those impulses from b and c which would otherwise give rise to sensations of green and violet respectively. With light of decreasing wave length below about 5900 Å the stimulation of a would rapidly fall off with decreasing wave lengths: this decrease in stimulation of a would account for the maximum of wave length discrimination in the "yellow."

"Green" light would stimulate b and c thus raising the threshold for the short as well as the medium wave length regions of the spectrum but the effect on the long wave length end would be limited to that portion of the total sensation of red contributed by the b and c receptors which would be stimulated by "red" light. The sensation of green would

[4] There are differences of opinion between various authors as to whether the receptor for short wave lengths represents one which gives rise to a sensation of blue or one which gives rise to a sensation of violet. For reasons to be given later the receptor will be assumed to be one for violet.

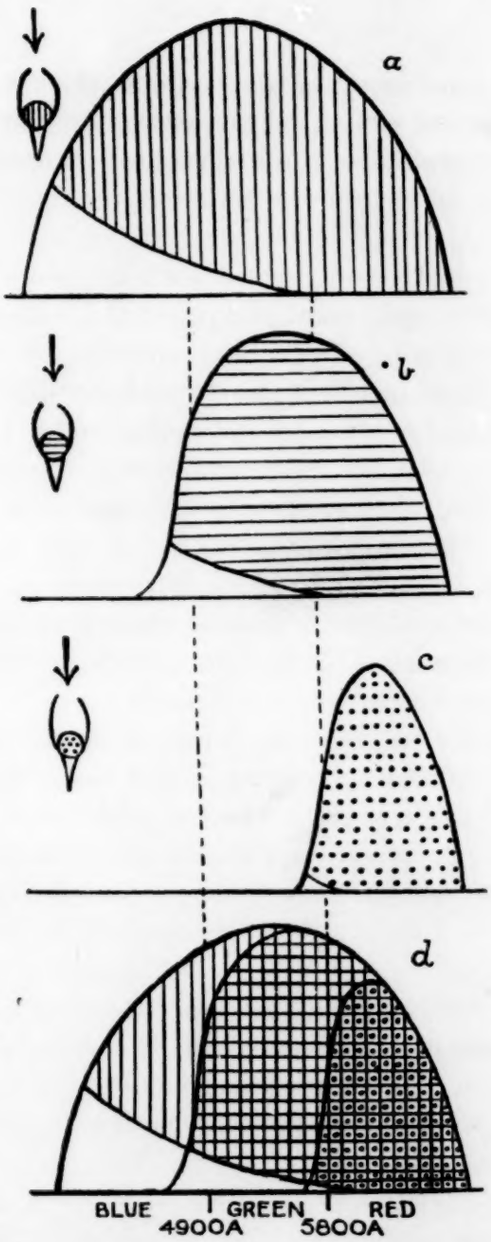

Fig. 3. *a*. Sensation curve for receptors sensitive to the whole of the visible spectrum. *b*. Sensation curve for receptors which fall off rapidly in sensitivity about 4900 Å. *c*. Sensation curve for receptors which fall off rapidly in sensitivity about 5800 Å. *d*. Superposition of the three sensation curves. The clear area indicates the photochromatic interval. The shift of the maximum intensity with increasing brightness may be due to stimulation of more than one set of receptors at the long wave length end of the spectrum. For the hypochromat the dots would be deleted leaving the other two sets of receptors active as in the "green" area. Insets: cones from hen's retina with correspondingly coloured globules. The arrows show the direction of the light. (Reproduced from Nature, 1930, cxxvi, p. 826.)

be accompanied by inhibition of those stimuli which would otherwise give rise to the sensation of violet. With decrease in wave length of light at about 4900 Å there would be a rapid decrease in the stimulation of b, thus accounting for the maximum of discrimination about that region of the spectrum.

"Violet" light would stimulate only the c receptors and the thresholds for "green" and for "red" would be interfered with only to the extent that stimulation of c entered into the thresholds for "red" and "green."

There are two ways in which this hypothesis differs markedly from the Young-Helmholtz one. The first is the inhibition produced by the sensation of red on those of green and violet and the inhibition of the sensation of violet by that of green. The second is that the sensation of white is due to unequal stimulation of the three receptors instead of equal stimulation of them as in the current view. Neither of these differences need be considered as making the hypothesis improbable. In fact, inhibition of impulses which ought to give rise to coloured sensations is found in binocular observations (see p. 74).

If the third receptor is really one which gives rise to a blue sensation the production of violet by a mixture of red and blue sensations can be easily explained If the a receptors are stimulated by the extreme short wave length rays (e.g., because the colour filters transmit some of those rays) the mixture of red and blue will be produced. A true "red" would be differentiated by the fact that the intermediate receptor would be stimulated as well.

It may help the reader if the relations between the receptors and the stimulating light are crudely represented in tabular form. To the left is represented the relation when the receptors represent sensations of red, green and violet: to the right, when they represent sensations of red, green and blue.

STIMULATING LIGHT	RELATIVE EFFECT ON RECEPTORS	RELATIVE EFFECT ON RECEPTORS
White	a < b < c	a < b < c
Red	a = b = c	a = b = c
Yellow	a < b = c	a < b = c
Green	b = c	b = c
Blue	b < c	c
Violet	c	a < c

This table is intended to represent the relative stimulation of the receptors by coloured lights. For instance, with "white" light the "red"

portion could act on all three receptors to its full intensity, the "green" portion could affect b and c receptors whilst "blue" or "violet" would act on only c. Therefore the relative stimulation of a is less than that of b which in turn is less stimulated than c.

As the result of dark adaptation the sensitivity of the c receptors will increase and on the extra foveal retina the influence of the c receptors will predominate hence the change of colour values in dim light and on the extra foveal retina (see p. 69).

The achromatic threshold may depend upon the sensitivity of the c receptor but for most people the sensitivity of the a receptor is close to that for c, hence there is a very small, if any, photochromatic interval with "red" light (20). The threshold for b is higher than that for c or the sensation of green is influenced to a considerable extent by impulses from the c receptors, hence the greater photochromatic interval and greater increase in sensitivity during dark adaptation for "green" than for "red."

The hypothesis is especially useful in explaining defects in colour vision. Absence of the a receptor would cause inability to distinguish between "red" and "green" but no change in sensitivity to light. Decrease in the specific discrimination of a would account for decrease in the discrimination between "red" and "green," as is found in minor degrees of hypochromatopsia. The second form of hypochromatopsia in which there is said to be a shortening of the "red" end of the spectrum was mentioned earlier (see p. 56).

The three types of receptors might be associated with three different photosensitive substances and in that form the hypothesis is no more improbable than the assumption of three photochemical substances of which the sensitivity is represented by the Young-Helmholtz, Hecht, or other curves.

Another view is that advanced by Schultze (106) that the discrimination of colour depends upon colour filters in front of the receptors. In this case the one photosensitive substance, visual purple, would be sufficient to account for all stimulation of the receptors, a view at first supported by Hecht (50) and Hecht and Williams (59) but abandoned later by Hecht (58, p. 36).

Colour filters are present in the cones of amphibians, reptiles, birds and marsupials (106, 133–146) Their presence in the cones of the bird's retina can be demonstrated by the simple process of spreading on a slide the retina from a freshly killed bird and examining it with the low power of a microscope. In the case of *Gallus domestica* red, yellow and almost

colourless oil globules are present. The light transmitted through these is of just those qualities which would account for the behaviour of the a, b and c receptors mentioned above (142).

There are several reasons why such filters may have escaped detection in the higher mammals. First, domestic animals may not recognise colours. Pavlov states that it is doubtful if reflexes depending on the recognition of colour can be developed in dogs. Secondly, the cones of mammals are much smaller than those of birds and any process of paraffin of celloidin imbedding would dissolve out fat globules. It is probable that the globules might be found only in the fovea of man or of the higher apes.

On the other hand the presence of the yellow spot in man indicating a decreased sensitivity to "blue" would be expected if red and yellow filters were present in that area.

The physiology of the coloured globules in birds need not be discussed here as it does not matter whether they help in "distance vision" (137, 139) or are for colour recognition. As the coloured oil globules are situated at the junction of the cones with the cone bodies light must pass through the colour filters before it reaches the cones. Therefore it is clear that in the retina of animals in which such globules are present certain cones can be stimulated only by the "red" of the spectrum, others by light from the "red" end down to about 4900 Å and a third set by the whole spectrum.

Parschin (81) has produced conditioned reflexes to coloured objects in turtles and he is investigating the possibility of the responses being due to differences in intensity. There is a possibility that the colour may become diffused throughout the cone and not confined to an oil globule as Dobrowolski (133) and Müller (141) found that the characteristic colour was also present in the cones.

It is unlikely that coloured globules will be found in the retina of the human eye. What is meant to be emphasised is the apparent similarity between the experimental work described above and the results which would be expected from the presence of such globules. For example, the coincidence of the maxima of discrimination with the absorption limits of the coloured globules from the retina of the domestic hen and the irreciprocal relation between the two ends of the spectrum. A new point of view is required and it is advantageous to see that at present there are several alternative explanations possible, such as those of Hecht and Roaf.

Duplicity theory and functions of the rods. The presence of two kinds

of receptors led Schultze (106) to suggest that they had different functions depending upon the intensity of the light. This hypothesis was developed by Parinaud (82) and von Kries (69). The human retina is peculiar in that although rods and cones can be recognised in the extra foveal retina the fovea contains structures which are intermediate in structure (41, 104). Therefore one cannot speak of a rod free area meaning one without the function of rods (83, p. 12).

The principal points in support of the duplicity theory are that vision in dim light is monochromatic (bluish white (70)); that the extra foveal retina is more sensitive than the fovea in dim light and that rods predominate over cones in the extra foveal retina.

The same facts have been interpreted by Konig (66) and Sivén (108) in favour of the rod being responsible for colourless (bluish) vision in dim light and for recognition of blue at higher intensities. This view has much to recommend it. Monochromatic vision in dim light is bluish and the greatest increase in sensitivity during dark adaptation is for "blue" light.

If the rods were the c receptors the explanation of colour vision could be simplified because instead of four receptors demanded by von Kries (69) one for achromatic scotopic vision and three for chromatic vision, it would be necessary to have only three, namely, rods for achromatic, scotopic and blue vision and the a and b receptors which could be cones.

We have had reason above to suggest that the c receptor is stimulated by the whole spectrum. Further evidence on this point is furnished by the phenomena of the effect of slightly oblique stimulation of the retina with a small source of pure "red" or "green" light. The coloured spot has surrounding it or, leading off from it, a violet halo or violet arcs. This phenomenon has been called secondary excitation of the retina (14, 29, 73, 116) but it is more probably due to stimulation of the extra foveal retina with the halo from the image of the small source of light (99). The frequency with which a violet mist is seen during experiments with the dark adapted eye is further evidence that the c receptor is stimulated by all regions of the spectrum. It is because of this appearance of violet that the reviewer has considered violet as the sensation produced by the receptor which is the only one stimulated by the short wave length end of the spectrum.

The observation of Hartridge (44) that a blue sensation can be produced by light which does not contain any rays of shorter wave length than 5300 Å is additional evidence that the receptors for "blue" can be stimulated by longer wave lengths.

The experiments on acuity of vision previously mentioned above suggested that the receptors for "blue" were of a different nature from those for "green" or "red." This peculiarity could be explained by the histological arrangement whereby the rods are united in groups to a single ganglion cell.

Another point in favour of the rods being the receptors for blue or violet vision is in relation to night blindness.

A full discussion of blue blindness is given by Köllner who points out the close relationship between blue blindness and night blindness. Due to the courtesy of Mr. T. C. Summers and Dr. W. S. Duke-Elder the reviewer has examined 5 cases of retinitis pigmentosa and in each case there was evidence of decreased sensitivity to light of the whole spectrum but particularly of the "blue" end (101, p. 290, and unpublished cases). These cases made mistakes in the naming of blues and greens as well as in those colours bordering on yellow (65 p. 49). If the rods are particularly affected in retinitis pigmentosa then there is evidence that the rods are related to the recognition of blue. The literature on night blindness (147–164) is mainly concerned with measurements of visual fields. In the majority of records it is stated that the fields for blue are diminished. Of course the degree of the defect will vary and one must not expect to find a marked degree of blue blindness when there is only a slight or doubtful extent of night blindness.

Although there is a prima facie case for the rods being concerned in violet vision we must remember that the structures in the fovea are neither ordinary rods nor ordinary cones (83, p. 12).

Naturally a yellow pigment (such as that of bile) will cause blue blindness by absorption of light of the shorter wave lengths and as adaptation is largely due to increased sensitivity to "blue" adaptation will also be decreased. Such cases need not have anything to do with the functions of the rods but in some cases (e.g., bile salts) visual purple may be dissolved out of the rods. Santonin may produce its effect either by the yellow pigment derived from it or by some action on the nervous system (109, 110).

The photochromatic interval and the change in sensitivity during dark adaptation both show that the green sensation is more closely related to the blue than to the red sensation. Different individuals do not have the same sensitivity to coloured lights. Abney and Watson (2, 4, 121) showed that there were at least two classes of individuals differing in their sensitivity to green.

Some observers do not see any photochromatic interval with red light or with any light on the fovea (20).

Miss Wentworth (122, p. 181) finds that the fovea of her dark adapted eye is less sensitive to all colours than is the extra foveal retina whilst for the reviewer the fovea is always more sensitive to "red" than the extra foveal retina.

The close relationship between "green" and "blue" may be due to the c receptor having a great influence on the sensation of green.

Extra foveal vision. The colour vision of the extra foveal retina differs from that of the fovea. This difference is generally ascribed to the decrease in the number of cones and an increase in the proportion of rods from the fovea to the extra foveal parts of the retina. The recognition of colour on the extra foveal retina depends upon the intensity of the light and the area of retina illuminated (Baird (15)). Feree and Rand (30) and Wentworth (122) have determined the threshold energy value for colour recognition and the latter has made measurements over her whole visual field.

Lythgoe (75) has examined the colour recognition of five subjects on stimulation of the extra foveal retina under conditions of both light and dark adaptation. He does not state whether the intensity of the light was corrected for decrease in the effective area of the pupil due to the varying degree of eccentricity. With the light adapted eye all the colours, with the doubtful exception of yellow, became darker with increasing eccentricity. This effect might have been due to the decrease in effective aperture of the pupil. With the dark adapted eye the colours became less saturated with increasing eccentricity. He explains that this change in saturation is due to the predominance of rod vision in the extra foveal retina. The light is first colourless then blue as the intensity rises above the photochromatic intervals. Further in towards the fovea other receptors come into action with the appearance first of a common red-green or yellow sensation, then the red sensation. These changes in colour can be explained on the basis that the a and b receptors are distributed in decreasing numbers away from the fovea. With the light adapted eye the rods are less sensitive hence the true colours are easier to recognise.

The extreme sensitivity of the rods in the dark adapted eye may give rise to false sensations. When first awaking in the morning and looking at a bright light, such as a narrow chink in the curtains, a violet colour is seen if the light is looked at for only a very brief interval.

Kleitman and Piéron (64) and Piéron (86) measured the duration and intensity of a light which would just suffice to stimulate the retina. They found that the product of intensity and duration gave two minima

at durations of 80σ and 2σ for the fovea. For the extra foveal retina "red" differs from "blue" the former behaving like "white" does at the fovea whilst the latter has a minimum product about 2σ. This result again suggests that there is a different type of receptor for "blue."

Previous exposure to high intensities of coloured light alters the sensitivity of the retina and attempts have been made to explain defective colour vision in terms of such reduced sensitivity. Burch (19) described the changes in colour of the spectrum after his eye had been exposed to bright light from restricted regions of the spectrum. Porter and Edridge-Green (88) observed the changes in the spectrum after fatigue to narrow regions of the spectrum. Hollenberg (62) studied the changes in "flicker" experiments. Hamilton and Laurens (42) measured the discrimination of colour after previous exposure to bright lights. Such explanations are not satisfactory because a marked decrease in sensitivity is always produced and that is not always the case in defective colour vision. Of course the ratio of stimulation of the different receptors will be altered by previous or simultaneous exposure to light. This problem has been discussed above (see p. 51).

The section on interpretation indicates that we can explain colour vision on the assumption that there are three sets of receptors which we have designated a, b and c. Diminution in specificity of a, such as by decrease in concentration of pigment, will give rise to varying degrees of of difficulty in distinguishing between "red" and "green." For instance, even if the red globules were so pale as to be yellow there might still be a slight differentiation between "red" and "green" owing to the c receptors having a relatively greater influence during stimulation by "green" than by "red" light.

The difference between the two types of red-green confusion may be due to variations in the relative sensitivity of rods and cones. During dark adaptation visual purple accumulates. The rods contain large quantities of it whilst in the cones the amount, if any, is so slight as to escape detection. With increase in concentration of visual purple the threshold to light must fall. Now the rod function extends over the whole spectrum hence anomalous trichromatism and the two forms of red-green confusion may be due to the influence of rods. Preliminary experiments indicate that the ratio of "red" to "green" required to match a heterogeneous yellow differ in the light and dark adapted conditions. It is of interest in this connection that the Purkinje phenomenon is absent in night blind cases (83, p. 222).

PSYCHOLOGICAL ASPECTS. Although the recognition of colour is a

psychological problem this review would have ended with the consideration of the kinds of receptors present in the retina had not certain problems required a brief consideration in order to complete the review of the subject.

If vision is based upon nerve impulses from three different sets of receptors we must correlate the simple sensations with the receptors. As the number of simple sensations exceeds the number of receptors some apparently simple sensations must be due to impulses passing up from more than one variety of receptor.

The modifications in sensation due to contrast must also be considered as they are such well known phenomena and ultimately their explanation must be included in any comprehensive view of colour vision.

Finally binocular combination modifies colour sensations and evidence can be furnished by binocular experiments which is useful in considering the interpretation of the sensations produced by stimulation of the receptors.

Impulses initiated in the receptors pass through a chain of cells in the retina. As the retina is an outgrowth from the cerebral cortex it is to be expected that some of the processes such as summation, occlusion and inhibition in the retina will be similar to those in the cortex. Granit (33–40) is making a study of such processes in the retina.

Öhrwall (80) has proposed a scheme whereby the sensations can be accounted for on the basis of three sets of receptors in the retina.

Colour sensations. The psychologically simple colours are red, yellow, green, blue, white and black. Three of these are additional to those corresponding to the regions of the spectrum demarcated by the maxima of discrimination. If the sensation produced by stimulation of the short wave receptor is violet, the blue is another simple sensation not related to a separate receptor and the complex colour violet (red blue) is related to a receptor of its own.

The production of a sensation of yellow has been one of the stumbling blocks to an understanding of colur vision. That a sensation of yellow can be produced by binocular combination of "red" and "green" light is proof that the simple sensation can be produced by heterogeneous stimuli (see p. 60). Further Edridge-Green (26) has shewn that two yellows, one produced by stimulation with "yellow" light and the other by a combination of "red" and "green" lights, both show the same changes in appearance after the retina has been fatigued to either "red" or "green." The reviewer has repeated these observations with spectral lights and agrees that fatigue to "red" causes both yellows to appear less

intense and greenish whilst fatigue to "green" causes both yellows to appear less intense and reddish. Edridge-Green maintains that the two yellows are different but the reviewer concludes that they are identical.

The sensation of white can be produced by heterogeneous stimuli and no homogeneous stimulus will give rise to a sensation of white (except the bluish white of achromatic scotopic vision). If white is a simple sensation produced by heterogeneous stimuli it does not seem to be impossible that the simple sensation of yellow is also the result of stimuli carried up more than one group of nerve fibres even when the stimulus is a monochromatic "yellow" light.

The sensation of blue can be produced by "green" and "violet" stimuli so that even if there is no special receptor related to blue sensations the facts can still be explained on the basis of a trichromatic hypothesis.

The sensation of black is always associated with a *relative* deficiency of stimulation. Thus a mixture of black with a spectral colour cannot be produced merely by decreasing the intensity of the illumination. But if the intensity of a spectral "red" is reduced and at the same time a bright spectral light (e.g., yellow) shines alongside the spectral "red," the red appears as if it were a rich brown.

The influence of differences in brightness on colour comparisons has been mentioned earlier (97) (see fig. 1).

Adrian (6, p. 114) and Roaf (95, p. 378) have proposed that the intensity of a sensation depends upon the number of impulses passing up a nerve fibre in unit time. By stimulating more nerve fibres the number of impulses reaching the nervous system is increased and although referred to a larger area the intensity is judged to be greater, this misjudgment is known as extensity and an example is the improvement in colour recognition on the peripheral retina with increase in area of illumination (15).

The bearing of the above paragraph is recognised in relation to mixed colours. For example, if a yellow sensation is due to a certain ratio of impulses passing up from a and b receptors then a relative increase in the number of impulses passing from the a receptors will cause the colour to appear more orange and a relative increase in the number of impulses passing from the b receptors will cause the colour to appear greenish. Some such relation must be postulated if we are to explain colour vision on the basis of a limited number of receptors.

Simultaneous contrast. Colour contrast is another thorny subject which must be firmly grasped. The recognition of colour differences depends on the relative frequency of impulses from the various receptors.

There is no fixed standard for the recognition of the black-white series, thus a piece of paper appears white even when illuminated by light which is not of the daylight standard of whiteness.

If two sources of illumination shine simultaneously on a "white" background and if they are of different qualities an upright rod will cause two shadows of different colours. If one is a colourless light such as daylight or some special "day light" lamp and the other is yellowish such as a candle or carbon filament lamp, one shadow will appear yellow and the other blue. The first shadow is yellow because it is illuminated only by the yellow light whilst the other shadow should be colourless as it is illuminated only by the colourless light. The appearance of blue in the latter is due to the fact that the white background is really slightly yellowish, being illuminated by both the colourless and yellow light, therefore the shadow from which the yellow is screened is less yellow than the apparently white background. If the slightly yellow background is judged to be white the less yellow shadow must be considered to be of the complementary colour to yellow that is blue.

A similar explanation can be given for the colouring of a grey strip on a coloured background the whole being covered by some semitransparent material. The grey strip with its overlying material reflects much less light of the colour of the background than comes from the background with its overlying material. The overlying material is thought to be white hence the relative deficiency of the background colour is judged to be due to the strip being of the complementary colour of the background (25), (27, p. 233) 8 (238).

Successive contrast or induction. A positive after image, that is, one of the same colour and light and shade effect as the original can be due to the persistence of the stimulating effect due to the products of photochemical decomposition. Positive after images are not seen at all times because subsequent stimulation of the eye causes their obliteration.

A negative after image, that is, one in which complementary colours are visible and the light and shade effect is reversed, can be explained as due to removal of photosensitive substance by previous illumination. On looking at a neutral surface the receptors in which the photochemical substance has been diminished will be stimulated to a less degree than the others hence the sensation will be largely due to those receptors which had been less stimulated previously, that is, the colors will be complementary and light and shade effects reversed.

Such a simple photochemical explanation will not, however, explain many of the phenomena of after images (19, 79, 92) hence one has to

assume the existence of a process of induction whereby the sensitivity of the retina is altered. The burst of impulses produced when light is cut off from the retina (83, p. 18) and the "self light" of the retina show that the processes are more complicated than can be explained by the brief statement above.

Binocular vision. The interest in binocular vision for this review is that it shows the possibility of the inhibition of impulses somewhere beyond the retinal receptors. In the case of "rivalry" and in Hartridge's interesting experiment (43) the two eyes are separately stimulated but the sensation may be that of only one eye or parts of the field of each. Therefore we must not expect to interpret colour vision in terms of retinal processes alone.

Sherrington's interesting binocular flicker experiments, (107) although not concerned with colour sensations, show that each eye with its attendant nervous connections can elaborate complete sensory images and that combination must occur at some still higher level. It is probable that inhibition occurs at that higher level.

The influence of psychological factors in colour vision cannot be overlooked. If one really believes that impulses from three sets of receptors can account for colour sensations we must be prepared to show that the three sets will account for the facts. Adaptation may be mainly due to changes in the amount of photosensitive substance in the receptors. Thus the effect of simultaneous exposure to two lights may produce a change in threshold by bleaching photochemical substances. On the other hand exposure of neighbouring areas may produce an effect by summation, occlusion or inhibition thus producing a change in sensitivity known as induction.

I have much pleasure in thanking my assistant, Dr. C. E. Brunton, for much help and criticism during the writing of this review.

The reviewer has indulged in speculation in order to show that it is possible to regard colour vision from a comparatively simple photochemical point of view. A working hypothesis is useful to coördinate data and to suggest problems for further investigation.

The old battle between the Young-Helmholtz and Hering hypotheses is finished. If new battle cries are raised it is hoped that the munitions will be furnished by experimental evidence and that the hypothesis will not be considered to be the test of the validity of the results.

ADDENDUM. After this review was written a book by Houston[5] was published. On the last page of the book he gives an excellent summary of some of the views expressed in this review and criticises them by saying "Roaf's theory of colour vision is open to the same mathematical objections as the Young-Helmholtz Theory."

It is rather premature to attempt to reduce the hypothesis to mathematical accuracy but the main objection to the theory is that no one has shewn either three photosensitive substances or colour filters in the human eye.

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METHODS

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Night blindness and blue vision

(See also (65) Köllner)

I have much pleasure in thanking Miss K. Tansley for a number of these references.

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In June, 1932, a discussion on vision was held jointly by the optical and physical societies of Great Britain. When the discussion is published it should be consulted by all those interested in vision.

POSITIONAL ADJUSTMENTS OF THE PRESSURE OF THE CEREBROSPINAL FLUID

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One of the many physiological problems involved in the adoption of the erect posture by certain of the vertebrates is that related to pressures about the central nervous system. In the primitive four-footed animals no part of the central nervous system is carried at a much higher level than any other, but as evolutionary development led into different habits and into different modes of progression, the head-end of these vertebrates became carried customarily above the rest of the body. Present-day vertebrates, in the four-footed series, show this elevation of the head to various degrees; in the fossil reptiles, particularly those with very long necks, the phenomenon was outstanding. But in all the fossil and existent vertebrates, the elevation of the head apparently reached its most extreme degree in the giraffe with its inclined vertebral column and its excessively long cervical region. Among the other mammals this tremendous difference in levels about the nervous system is not encountered, but within this class of vertebrates there are many examples of postural habits of extraordinary variety.

Among the birds also the elevation of the head of the animal above the rest of the body may be very marked indeed. This is true not only in those birds with normal semi-erect postures, but also it is true in those whose anatomical differentiations have resulted in extreme length of neck. Evolving in a highly specialized way from some ancient reptillian stock the birds show far less of a four-footed architecture today than do our mammalian forms.

Within the mammalian class there exist today many four-footed animals whose heads are only infrequently carried at levels differing markedly from those of their almost horizontal spinal cords. The power of elevation or depression of the head is however essential for the protection of the animal and for the acquisition of food; and in climbing or rearing the entire animal may be so inclined, for short periods, that one end of the central nervous system is high above the other. In the primate order, there are many monkeys whose habitual posture is almost erect

even though progression remains for them a four-footed phenomenon. Again, there are the brachiators whose normal method of progression is by swinging from branch to branch of trees; here posture is essentially erect. In the great anthropoid apes, progression may occasionally be of the erect type and with these the sitting posture is erect as it is in the new and old-world monkeys. In man, progression is of course bipedal and erect; during his waking hours man carries his head more or less vertically above his vertebral column.

Such semi-erect and erect postures as have been developed within the mammalian group have necessitated physiological adjustments within the fluid-systems of the body. In particular the vascular system has made the necessary functional changes assuring an adequate arterial supply to the cerebral hemispheres, with the development of vasomotor control fairly well suited to the purpose. On the venous side also, the caliber of the vessels may be markedly altered by nervous impulses, and the active functioning of valves interrupts the continuity of potential fluid-columns. These mechanisms acting within the blood vascular system are fairly well understood, but similar knowledge does not exist regarding the hydrostatic changes in the pressure of the cerebrospinal fluid which so completely fills the cerebral ventricles and surrounds the nervous system in the subarachnoid space.

The problem of pressure-alterations about the mammalian nervous system, in the change from the horizontal to the erect position, becomes somewhat more understandable if certain anatomical characteristics are recalled. The subarachnoid space, existing between the pia mater and the arachnoid membrane, is traversed by numerous trabeculae, but the meshes of the space freely communicate with each other so that a continuous column of cerebrospinal fluid exists. There are within the subarachnoid space no anatomical structures which could even remotely be considered to serve as functional valves. The caliber of the space varies greatly in different parts of the nervous system, but this variation does not affect its hydrostatic effects. Outside of the arachnoid membrane is the dura mater—a tough, relatively non-distensible membrane, adhering closely to the skull in the cranial portion but suspended as a tubular envelope within the epidural space of the vertebral canal. The epidural space is filled, in the mammals, with a fatty areolar tissue in which is embedded a large and extensive plexus of thin-walled veins. This tissue appears to increase in volume, relative to the spinal dural sac, from infancy to old age.

With such an arrangement of membranes and fluid-spaces about the

nervous system, with the cerebrospinal liquid free to circulate everywhere in the subarachnoid space, it is perhaps surprising that more efforts have not been made to ascertain the effect of changes in posture upon the pressures existing around the nervous system. For the question naturally arises as to whether the full height of the spinal and cranial columns of cerebrospinal fluid is effective in modifying the existing positive pressures of the horizontal position when the mammal assumes the erect posture. Yet in one way it is not surprising that more specific efforts to learn the physiological mechanisms of these pressure-effects have not been made when one realizes that thought in this field has been more or less continuously dominated by a doctrine a century and half old. Any discussion of the problem of hydrostatics of the cerebrospinal fluid necessarily gives full weight to this hypothesis of constant volume within the coverings of the nervous system.

In 1783 Alexander Monro (18) first promulgated the thesis that the blood circulating within the cranium must at all times be constant in volume. Monro's reasoning was that "as the substance of the brain like that of other solids of our body, is nearly incompressible, the quantity of blood within the head must be the same, or very nearly the same." The basis for this hypothesis was Monro's anatomic generalization that the brain is "enclosed in a case of bone;" and it therefore followed logically that within a rigid-walled container, such as the cranium, the contents must at all times be of the same volume. Considering the volume of the brain to be unchanging and having knowledge of only one fluid element, Monro was necessarily led to the assumption of a constant intracranial content of blood.

Monro's concept, developed further by Kellie (13) so that it has come to be known as the Monro-Kellie doctrine, has not descended through one hundred and fifty years without additions and amendments. Burrows (4) was the first to introduce the cerebrospinal fluid into the doctrine; and while his findings were somewhat at variance with those of Kellie, he accepted the basic reasoning of the thesis, assuming a constant intracranial volume and making the blood and cerebrospinal fluid the two variable elements.

Originally restricted to the cranium, the doctrine of a rigid container for the central nervous system with a fixed and constant capacity has been necessarily extended to include the vertebral portion of the system. This modification was essential when it became generally appreciated that the cerebrospinal fluid of the spinal subarachnoid space communicated freely with the cerebral ventricles and cerebral subarachnoid

space (Key and Retzius, 14). The vertebral arches were then looked upon as affording the necessary rigidity for firm suspension of the spinal dural sac. The Monro-Kellie doctrine thus came to be interpreted as the concept which viewed the entire central nervous system as being enclosed within a bony container (cranium and vertebral canal) of sufficient rigidity to secure a constancy in volume of its intradural contents. Such an idea of constancy of the intradural contents involved appreciation of the anatomical relationships within the whole cranio-vertebral system, and it was intimately related to the integrity of the skull and of the vertebral column whose relative rigidity was held to modify in essential ways the spinal dural component. In this amended form, the Monro-Kellie doctrine of a rigid container of fixed volume has really afforded the basic thesis for all studies upon the pressure and volume-relationships about the nervous system.

As such a concept necessarily affects all ideas of possible pressure-changes in the cerebrospinal fluid on alteration of the animal's position, it seems desirable to analyze the type of evidence upon which the doctrine has rested. While presented by Monro on a purely anatomical argument, Kellie added evidence of similar intracranial volumes of blood *post mortem* in animals suspended by ears or by tails. These experiments, repeated with slightly different findings by Burrows, furnished a type of physical data to the problem; they were followed during the next few decades by attempts to examine the conditions of intracranial blood flow through windows inserted into the calvarium. Such observations as could be made by this method, in the hands of a fairly large number of investigators, notably Donders (6), and also Kussmaul and Tenner (17), were necessarily performed without control of all the factors, though the attempts represented distinct advance over the experiments on dead animals. The procedure permitted observation of only limited areas of the superficial vessels of the brain: they gave no information regarding changes in other portions of the central nervous system, in the internal vessels, nor in the most essential part—the capillary bed. The data gathered from these observations through a cranial window hardly justified the conclusion of a variable intracranial blood volume. Many years later (1896) Leonard Hill (12), employing more satisfactory methods of physiological control, came to the conclusion that "the volume of the blood in the brain is in all physiological conditions but slightly variable." Hill's deductions, based primarily upon studies of the pressures of the intracranial blood vessels and of the cerebrospinal fluid, carried the problem somewhat further toward its ultimate solution, but they introduced certain elements of confusion.

Dixon and Halliburton (5), in the course of their studies of the cerebrospinal fluid, devoted themselves to a general consideration of the Monro-Kellie doctrine, using methods of study almost identical with those employed by Hill. Largely on the basis of their finding that the pressures of the cerebrospinal fluid differed from those of the torcular herophilii, they concluded that "the cranial contents cannot any longer be regarded as a fixed quantity without the power of expanding or contracting in volume." Such an assertion necessarily involved marked modification of the Monro-Kellie hypothesis: the closed box character of the bony containers of the brain and spinal cord would, in this interpretation, be replaced by walls of some elasticity permitting a definite volume-change within the dural sac. While Dixon and Halliburton established the important fact that the pressure of the cerebrospinal fluid may vary without an exact correspondence in the pressure of the great dural sinuses, they presented no evidence of volume-change within the cerebrospinal system.

The next step came during the course of an investigation to determine what agents might affect the volume of the central nervous system. It was ascertained (27, 28) that the intravenous injection of solutions whose osmotic pressures differed widely from that of the blood, markedly altered the pressure of the cerebrospinal fluid and changed the volume of the brain. Strongly hypertonic solutions, injected intravenously, caused a profound lowering of the pressure of the cerebrospinal fluid, frequently to negative values (i.e., below atmospheric pressure), and at the same time produced a striking diminution in the volume of the brain. These findings were quickly related to the Monro-Kellie doctrine of fixed intracranial contents, and particularly to that part of the hypothesis pertaining to the rigid character of the container. While it was apparent that the effects of the intravenous injection of such solutions were dependent upon interchange of water and salts between blood and nervous system with its fluids, it was obvious that negative pressures in the cerebrospinal fluid could only be obtained if the walls of the container were sufficiently rigid to withstand collapse when fluid was abstracted from the nervous tissues and from the cerebrospinal fluid—sufficiently rigid to prevent the direct application of the effect of atmospheric pressure upon the dural sac and its contents. Under these circumstances, with possibility of variation in volume of the brain, of the cerebrospinal fluid and of the intradural blood, the deduction naturally followed that the intracranial contents were of a relatively fixed volume; that the cranial and spinal dural sacs were

completely filled with blood, cerebrospinal fluid and central nervous system; that variations in the quantity of any one of these elements might occur, but that these variations were in part at least compensated for by reciprocal changes in the volume of one or both of the remaining elements.

The problem of reciprocal volume-adjustment within the cranio-vertebral system really dates back far into the literature of the subject of the cerebral blood vessels. Monro (18) in fact made a suggestion of such a reciprocal relationship as did Kellie (13), but their suggestions were restricted to a diminution of cerebral blood-volume in cases of intracranial effusion of fluid. A reciprocal relationship between arterial and venous volumes within the cranium was however developed from their generalizations. The first comprehensive statement should be attributed to Burrows (4) in his discussion of the Monro-Kellie doctrine, and his portrayal of the reciprocal volume-changes between blood and cerebrospinal fluid has remained accepted without essential modification. Recently the problem has been attacked by H. S. Forbes and Wolff (9, 10, 30) who have used an adaptation of the well-established method of study through an intracranial window. While Forbes and Wolff observed a diminution in caliber of the pial arterioles and venules in a dehydrated brain, Kubie and Hetler (16) were able to show that the capillary bed of the cerebral surface exhibited a marked dilatation in such experimental preparations. The flushing of the cortex under these conditions was extreme and provided evidence of the reciprocal vascular adjustment within the cranium, representing the compensation within the blood channels for the fluid withdrawn by dehydration. And similarly, findings of an increased intradural blood volume have been made chemically by Weil, Zeiss and Cleveland (29) after administration of strongly hypertonic solutions. The whole mechanism of reciprocal compensation for volume-change in one of the elements of the intradural contents is important for understanding of the problem of total volume-change within the system: it applies fundamentally to the interpretation of all of the experimental work upon the subject.

It should be realized that at the time of promulgation of the idea of reciprocal relationships within the dural sac, belief in the Monro-Kellie hypothesis was based in great part upon speculation; the later demonstration of the rigidity of the container really rested upon the evidence afforded by the negative pressures within the dural envelope, as obtained by the intravenous administration of strongly hypertonic solutions. This lack of experimental verification of the assumed function of cer-

tain elements in the system has been supplied by studies aimed largely at the determination of the limits of accuracy of the thesis. In the literature suggestions as to the importance of the cranial vault to the concept had been ventured—first by Kellie (13) who noticed that in a trephined animal (dura opened?) marked variation in the intracranial blood-volume occurred on change in the animal's position. Again Ecker (7) recorded in a trephined animal a marked diminution in cerebral volume on division of the carotid arteries. These observations contrasted strongly with the findings in animals with intact crania and led directly to an experimental approach to the problem (26). In the first type of procedure, the cranial vault was widely removed, leaving the dura intact but exposed directly to atmospheric pressure. On intravenous injection of large quantities of a strongly hypertonic solution, the pressure of the cerebrospinal fluid could not be reduced to negative values; a small positive level of fluid persisted, indicating the height of one cerebral hemisphere above the puncture-needle. The second type of experimental preparation consisted in the opening of the bony calvarium without injury to the dura mater, temporary closure of the cranial defect by a glass slide sealed in position, the intravenous administration of a strongly hypertonic solution, and when negative pressures of the cerebrospinal fluid were recorded, the abrupt removal of the glass slide so that the cranial dura was subjected to atmospheric pressure. Immediately the pressure of the cerebrospinal fluid ascended to positive values, the level again representing the height of the one cerebral hemisphere above the occipital needle.

These data indicated that within the physiological limits tested the cranium and vertebral column introduced a factor of rigidity into the system. Such elements as the possible vascular readjustments in the nervous system, the stretching of the epidural trabeculae and dilatation of the epidural venous plexus, the collapsibility or expansibility of the spinal dural envelope, the elasticity of the occipito-atlantoid ligament and the theoretically possible movement of fluid along perineural channels,—all factors which by their anatomical arrangements might possibly prevent strict interpretation of the rigidity of the coverings of the central nervous system—were not of sufficient physiological importance to force one to disregard the bony framework of the cranium and vertebral column as a closed container. All these potentially active factors seemed of theoretical rather than practical significance, but the experiments based on dehydration of the nervous system dealt with relatively profound changes and were not such as to give information of the potenti-

alities of these factors within less drastic limits. The mere presence of such mechanisms however suggested that the rigidity of the container of the nervous system might not be complete—that these anatomical arrangements, as well as the vascular components, might contribute an element of elasticity to the cranio-vertebral structures.

Search for a means of attack upon this problem of the potentialities of these elastic factors resulted in new methods of study, based on certain postulates. First of all it seemed obvious that the degree of rigidity of the bony cranio-vertebral canal would determine in some measure such alterations in the pressure of the cerebrospinal fluid as the assumption of the vertical posture had imposed upon the nervous system. Were the spinal dural tube so suspended within the epidural space that it could not collapse inward, were its fibrous architecture of such small elasticity that outward distensibility were hardly measurable, were the cranium with its adherent dura a rigid box-like container, and were the vascular regulatory mechanisms of the intradural contents so effective that no volume-change nor dislocation of blood would occur—if these suppositions were correct, the measurable pressures of the cerebrospinal fluid in the horizontal position would be reproduced in the vertical position of the mammal, for this assumed rigidity of the container for the nervous system would then be such as to prevent a dislocation of fluid from the uppermost portions of the system to the lowermost. Such potential dislocation of cerebrospinal fluid would be necessary for measurable alterations in pressure even though in such positional change the vertical column of molecules theoretically imposed upon the lowermost portion would undoubtedly effect a pressure-change within the fluid itself.

Some of these considerations had been advanced in 1892 by Grashey (11) in a monographic presentation of the hydrostatics of the cerebrospinal fluid in the vertical position. His studies were without observational data on man or experimental animals; they constitute therefore a purely theoretical analysis of the physical problems imposed by the fluid-column of the subarachnoid space, as well as that of the hydrodynamics of the cerebral circulation. As a hypothetic exposition of some phases of the problem, of the potential modifications of the hydrostatic effects through the elasticities of the vascular components, Grashey's contribution is of great value. A far simpler, purely physical representation of the cerebrospinal system has recently been described (23): the system is likened to a rigid tube, with ends closed by elastic membranes and completely filled by fluid. By decreasing the elasticity

of one of these membranes the level of atmospheric pressure is shifted toward the more elastic membrane. This theoretical concept, like those of Grashey's, is of value only if it serves to explain the findings in living animals under properly controlled physiological conditions.

This need for an experimental analysis of the potentialities of the hydrostatic factor in relation to the Monro-Kellie thesis has been met by a series of experiments involving tilting anesthetized mammals from the horizontal to the vertical head-down and tail-down positions (21, 22, 24). Most of these observations were carried out on dogs of a uniform size (weight, 6–7 kgm.) and the findings in this animal may be considered to be typical as the reactions in the cat and monkey are essentially similar though differing slightly in degree. In these dogs, the distance from the occipital protuberance to the last lumbar spine was in the neighborhood of 400 mm.; this measurement may be taken to be that of the height of the column of fluid which might exert a hydrostatic effect in the two vertical positions. The tiltings from the horizontal to the head-down position caused increases in the pressure of the occipital cerebrospinal fluid which averaged 104.9 mm. of normal saline solution. In the contrariwise tiltings, from the horizontal to the vertical tail-down position, an average decrease of 74.3 mm. was recorded in the pressure of the cerebrospinal fluid as measured in the occipital region. The changes in the carotid pressure (reflecting intracranial arterial pressure) were not of great significance during such positional alterations, but the head-down tiltings caused an average increase of 184.1 mm. in the pressure of the superior sagittal sinus and the opposite positional change, an average decrease of 79.7 mm.,—in each case, changes of greater magnitude than in the cerebrospinal fluid itself.

One other type of experiment, having significance in our discussion, has also been carried out (22). In this, the pressure of the cerebrospinal fluid was recorded in the occipital region and by lumbar puncture measurement was made in the lower spinal region. In the horizontal position the pressures in both manometers were the same, but when the dog was tilted to the vertical head-down position, the fluid in the lumbar manometer ran into the animal's subarachnoid space, to be followed by air. Under these circumstances, atmospheric pressure was directly applied to the cerebrospinal fluid throughout the lower spinal segments; the pressure-increase measured in the occipital manometer became approximately 185 mm. instead of the customary 105 mm. in the intact preparation.

These observations were followed by further experiments (23) in which the cranial vault was largely removed or in which laminectomy was performed through the lumbar and thoracic regions. With the pressure of the cerebrospinal fluid measured by an occipital manometer, both of these preparations exhibited normal levels of the cerebrospinal fluid in the horizontal position. In those dogs in which the cranial dura mater was widely exposed to the atmosphere, the head-down tiltings gave pressure-increases of the cerebrospinal fluid of the same extent as in the intact animal, but on tilting from the horizontal to the tail-down position the pressure of the fluid decreased only 56 mm. on the average (74.3 mm. in the intact dog). On the other hand, the laminectomized animal showed on the tail-down tiltings a pressure-decrease of the same magnitude as in the intact dog, but on vertical head-down tilting the pressure of the cerebrospinal fluid increased on the average 185 mm. as compared to 104.7 mm. in the intact dog. Of particular significance was the fact that in the laminectomized and lumbar-punctured animals, the increases of pressure on vertical head-down tiltings were identical with the pressure-increase in the superior sagittal sinus; the full effect of atmospheric pressure was operative through the lumbar needle and upon the exposed spinal dura mater while the increase in intracranial venous pressure may be taken to be a reflection likewise of hydrostatic pressures exerted through the soft parts of the body.

The data from these experiments may be interpreted as demonstrating that the vertebral arches and cranium have a definite physiological function in removing the central nervous system from the full effects of atmospheric pressure. They lead also to the assumption that within these bony coverings there are elements which lack rigidity, as an obvious dislocation of fluid occurs within the dural sac during such positional tiltings. To speak of such a lack of rigidity within the bony coverings is really another way of saying that the system possesses elasticity—an elasticity which permits a dislocation of fluid from one part of the subarachnoid space to another—not the maximal but a fractional dislocation, permitted by dilatation and compression of the intradural vascular bed, by inward collapse of the spinal dural sac with stretching of the epidural fibers and dilatation of the epidural venous plexus. The stretch of the spinal dura mater has been found to be so small as to afford a negligible expansibility.

The explanation for the phenomena of positional pressure-changes in the cerebrospinal fluid unquestionably rests in the dislocation of fluid coincident with the change of hydrostatic pressure, but the measurement

of the fluid's pressure with an open-end manometer of small bore in the customary experiment permits an external dislocation of fluid—an obvious change in volume either into the manometer from the animal's subarachnoid space or from the manometer into the subarachnoid space. The influence of this factor of fluid-dislocation has been studied in tilting experiments on the same-sized dog, with measure of the pressure of the cerebrospinal fluid by the bubble manometer (recording pressure without external dislocation of fluid) and by manometers of various bores (25). The pressure-alterations in the cerebrospinal fluid as recorded by the bubble manometer were slightly greater than those in the open-end 1 mm. manometer; and as manometers of larger and larger bore were used the pressure-changes became less and less in both positional tiltings. Calculations of the fluid dislocated into or from these open-end manometers showed that a larger and larger dislocation of fluid occurred in the larger and larger manometers, though there was an obvious limit to the volume displaced.

These determinations of the differences in volume of fluid displaced into or from the manometers were found to have a fairly constant relationship to the differences in pressure-change in any one animal on tilting. This relationship was expressed in a fraction designated as $\frac{dV}{dP}$, where dV represented the difference in the volume-changes on tilting, while dP represented the difference in the pressure-changes. With dogs of the same size (6 to 7 kgm.) a fairly constant value for the fraction $\frac{dV}{dP}$ was obtained from the results of tilting to the vertical head-down and tail-down positions; in the whole series of animals the fraction $\frac{dV}{dP}$ was found to have an average value of 0.17.

From these findings there was developed the general thesis that the coverings of the central nervous system may be likened to a container of unknown volume with elastic elements of an unknown coefficient of elasticity. An evaluation of this elasticity of the dural sac and its contents has come through the application of the physical laws of an elastic system to the problem. The expression for any coefficient of elasticity is given as the quotient obtained by dividing the stress by the strain: in the coefficient of volume-elasticity E, the stress is the change in pressure dP, and the strain is the change in volume dV divided by the original volume V, or E = coefficient of elasticity = $dP/\frac{dV}{V} = \frac{dP}{dV}V$.

The elasticity of the dural sac and its contents may be taken to lead to a dislocation of fluid amounting to the volume dV which is related to a change in pressure dP. The ratio $\frac{dV}{dP}$, derived from the tilting experiments, may be considered to be equal to $\frac{V}{E}$, where V is the original volume of the fluid-system (intradural contents) and where E is the coefficient of elasticity of the membranes and vascular bed. This E is a general elastic coefficient for the system as a whole and should not be confused with the coefficient of linear stretch (Young's Modulus) of the membranes, and owing to the complexity of the system cannot be directly related to it. On the assumption that the volume V has a normal value in any one animal, the fraction $\frac{dV}{dP}$ might be expected to remain constant as long as the animal remained in good condition with normal responses. This expectation has been realized in this recent experimental work (25).

A similar relationship between pressure and volume of the cerebrospinal fluid is expressed in Ayala's (1) Rachidealquotient which he derived by dividing the difference between the initial and final pressures at lumbar puncture by the quantity of fluid removed. Ayala related his quotient to the volume of the cerebrospinal fluid and to the elasticity of the system; assuming that physiological elasticity does not vary greatly, he held the quotient to be an index of volume and found from his clinical studies an indication of smaller volumes in patients with brain tumor. As he dealt only with pathological cases the value of his quotient was not constant and the variations he found may have been due to changes in volume or to changes in both volume and elasticity.

As a logical outgrowth of the tilting experiments on dogs of a uniform size, came the determination of the general coefficient of elasticity of the dural sac and its contents in a series of dogs of different sizes and ages (8). The value of the fraction $\frac{dV}{dP}$ was first ascertained for the individual animal, and after death the contents included within the spinal and cranial dura mater were measured. In a series of dogs grouped as immature, young adult, adult, and old animals (weights, from 3 to 16 kgm.), the fraction $\frac{dV}{dP}$ was found to have values between 0.132 (immature dog) and 0.272 (old dog), while the intradural volumes in the same series of 20 dogs ranged between 60.8 cc. and 105.1 cc. There was

apparently no relationship between spinal length (occipital protuberance to last lumbar spine), body weight and intradural volume. Calculations of the coefficients of elasticity were made by substituting the values of $\frac{dV}{dP}$ and of intradural volume V in the formula $\left(E = V\frac{dP}{dV}\right)$: the various groups of dogs showed an extraordinary constancy in the magnitude of this coefficient of elasticity. The immature group had an average coefficient of elasticity of 4.58×10^5 dynes per cm.^{2}; the young adult group, 4.22×10^5 dynes per cm.^{2}; the adult group, 4.03×10^5 dynes per cm.^{2}; and the old group, 3.81×10^5 dynes per cm.^{2} The range of variation from the average was most extreme in the group of dogs classed as young adults, but even in this group the extremes were 4.09×10^5 and 4.39×10^5 dynes per cm.^{2} In spite of the difficulty of classifying dogs according to age, only one animal out of 20 was obviously out of line; this dog was grouped as an adult but its coefficient of elasticity would place it in the series of young adults.

One finding of particular importance to this discussion was that the values of the fraction $\frac{dV}{dP}$ were approximately the same whether derived from the pressure and volume-changes for the tail-down tiltings or from those for the head-down tiltings. This general equality of values held for most of the dogs in the series but occasional animals, (1 out of 5) showed head-down values for the fraction $\frac{dV}{dP}$ which were the same as the average values obtained from both types of tilting, while the tail-down values were usually of one-half the magnitude.

Similar determinations of the coefficient of elasticity of the dural sac and its contents have been made upon cats and macaques (24). The cats on such tilting experiments yielded data which placed the coefficient of elasticity in the neighborhood of 3.5×10^5 dynes per cm.^{2} with range from 3.86×10^5 dynes per cm.^{2} in an immature animal to 3.26×10^5 dynes per cm.^{2} in an adult. In the various age-groups the cats showed the same type of constancy in the values of the coefficient of elasticity as did the dogs, and also the same equalities of the fraction $\frac{dV}{dP}$ on derivation from the head-down and tail-down tiltings. The small series of macaques thus far reported (6 Pithecus sinicus and 4 Pithecus rhesus) gave calculations of the coefficient of elasticity which varied from 5.15×10^5 dynes per cm.^{2} in a very young juvenile (relatively younger than any of the dogs or cats) to 3.74×10^5 dynes per

cm.^{2} in an old animal; the macaques, like the dogs and cats, exhibited identity of values of the fraction $\frac{dV}{dP}$ on head-down and tail-down tiltings. These findings permit the generalization that the coefficient of elasticity of the dural sac and its contents is of the same magnitude in the dog and macaque throughout equivalent age-groups, but it is slightly less in the cat.

It is probably of some significance that a physical formula, used for the determination of the coefficient of elasticity of solids, fluids and gases on compression, could be applied with profit to the problems of meningeal elasticity so that the relationship of external dislocation of cerebrospinal fluid to its resultant pressure might be expressed as a fraction $\frac{dV}{dP}$, with a constant value for any one animal. In the case of the central nervous system it is apparent that the phenomena under consideration are not those of compression of the contents of the intradural cavity nor those of possible dilatation of these contents under conditions of reduced pressure. It seems clear that the changes in volume with pressure are due to the elasticity of the membranes and vascular bed which permits not only an internal shift of fluid from one part of the nervous system to another but also an external dislocation into or from manometers during positional change. It is surprising that the total effect produced by a complex system containing elements with different degrees of elasticity can be expressed by one general coefficient of elasticity which is so nearly constant in animals of the same species, even though differing greatly in age and size. Were intact animals to be tilted from the horizontal to the two vertical positions, an internal dislocation of fluid would unquestionably occur but it would occur without any appreciable change in the total volume of the intradural contents. In the experiments employing open-end manometers, the total volume of the intradural contents may be taken to vary, at the maximum, only to the extent of the amount of dislocation of fluid into or from the external system: any intradural volume-change is at least in part compensated for by reciprocal variation in the total amount of blood within the dural sac. This reciprocal readjustment in the intradural vascular volume cannot be complete or the total volume V would not vary by the amount dV and the formula for elasticity could not be applied.

Although the pressure and volume-changes within the cerebrospinal fluid alone were determined in the experiments dealing with abrupt posi-

tional tiltings, it should be pointed out that the fluid here merely portrays the intradural alterations. The pressure-change, while existing within the fluid itself, is actually reflected by the fluid upon all of the intradural structures so that all parts of this central nervous system are affected in some way by the recorded change. Somewhat similarly the volume-change represents not an alteration in the total volume of the cerbrospinal fluid but an alteration in the total volume of contents of the entire dural envelope, whether of the nervous tissue itself, blood vascular bed, or of the cerebrospinal fluid.

The data obtained from all of these observations dealing with the abrupt tilting of mammals from the horizontal to the two vertical positions really allow a re-casting or re-statement of the Monro-Kellie doctrine. Interpretation of the experimental findings leads to a conception of the central nervous system being surrounded by membranes and vascular channels possessing elasticity. The intradural cavity may be taken to be completely filled by central nervous system, by blood, and by cerebrospinal fluid; its volume is, under normal conditions in the intact animal, apparently constant. The cranial walls and the vertebral arches may be looked upon as affording rigidity to the whole system and as protecting it from atmospheric pressure, but there is within this bony container a complex elastic element, constituted of the spinal dural sac and also of the blood vascular channels within the nervous system and the meninges. This elastic element permits, in the intact animal, a dislocation of fluid from one part of the nervous system to another without appreciable change in volume. When however the volume is altered by external displacement of fluid the elasticity of the system permits this external dislocation as well as the internal readjustment of the fluid volumes. The experiments performed on dogs, cats and macaques indicate that the coefficient of elasticity of the dural sac and its contents in these three mammals is of approximately the same magnitude; and it seems fair to conclude that somewhat similar values may be found to hold throughout the mammalian class.

It should be pointed out again that the coefficients of elasticity referred to above represent values derived from the volume-changes into or from external systems as well as from the changes in pressure which affect both external and internal conditions. But as these coefficients are calculated from data furnished by tiltings where there is no external volume-change as well as by those in which there is a progressive increase in the volume dislocated, it appears logical to assume that these coefficients in dynes really serve as a measure of the power of the dural sac

and its contents to resist deformation or of the power to restore the original form after deformation. The experiments with tilting from the horizontal to the two vertical positions unquestionably fall within the normal limits of the elastic system; the two vertical positions may represent abnormal or seldom employed postures for the individual animals but they are within the range of possible performance.

The dural sac and its contents apparently function as an elastic system only within a certain pressure-range. This limitation in elasticity is brought out with exceeding clarity in those experiments in which the intravenous injection of strongly hypertonic solutions has reduced the pressure of the cerebrospinal fluid to negative values. Here the increased osmotic pressure of the blood has abstracted fluid from the nervous system (and also from the cerebrospinal fluid) in amount beyond the collapsibility of the cranio-vertebral system. The functional modification placed upon the elasticity of the dural sac and its contents by the bony encasement of cranium and vertebral column then renders possible the existence of pressures less than atmospheric within the cerebrospinal fluid and those structures which it bathes.

Such reconstitution of the Monro-Kellie hypothesis in the light of recent work makes it feasible to assay the bearing of these findings and deductions upon the general problems of positional adjustment of the pressures about the mammalian central nervous system. The pressure-changes about the central nervous system on tilting represent pressure-changes which are accompanied by the dislocation of cerebrospinal fluid within its meningeal bed. The changes occur as internal dislocations of cerebrospinal fluid in the two vertical positions of the animal, the shift being from the highest parts of the nervous system into the most dependent. Shown clearly in the bubble manometer where pressures may be measured without external dislocation of fluid, these changes of dislocated fluid may be looked upon as primarily internal although they occur when an external dislocation of fluid is permitted. A maximum dislocation of the cerebrospinal fluid does not occur in these tiltings to the two vertical positions in the intact animal: only a proportion (one-third to one-fourth) of the total hydrostatic height of the spinal column of fluid is effective when the animal is tilted from the horizontal to the vertical head-down position and a somewhat smaller proportion is effective in the vertical tail-down tiltings. These phenomena mean that the elasticity of the system is modified in an essential way by the character of the bony coverings of the central nervous system and by the character of the suspension of the spinal dural envelope.

In view of these considerations and the experimental findings detailed in foregoing pages, the question naturally arises as to whether one should expect to find the uppermost portions of the subarachnoid space filled to more than capillary caliber when the animals are in the perpendicular positions. Experimental observations indicate that the changes in total volume are minimal or non-existent within the dural sac of the intact animal on tilting to the vertical positions, but when atmospheric pressure is allowed to act directly upon the cerebrospinal system actual volume-changes occur within the cranio-vertebral cavity. If the meniscus of fluid in the open-end manometer or in the reservoir of the bubble manometer be taken as that of atmospheric pressure, this level may be projected within the animal so that some information may be gained as to internal pressure-conditions. Thus with dogs in the head-down position, the meniscus of fluid will usually be 225–235 mm. of saline solution above the occipital needle (i.e., in the lower thoracic region). In the tail-down vertical position, the same process of reasoning projects the atmospheric pressure-level within the cranial region, usually about 50 mm. above the occiput. Above these levels of atmospheric pressure in these two vertical positions, the pressures in the subarachnoid space will be increasingly negative (less than atmospheric), the space apparently being reduced in caliber though with a dilated capillary and venous bed. The subarachnoid fluid-layer may be in places merely of capillary thickness; if this assumption be true, then information regarding the pressures existing within it may be entirely hypothetical as such a capillary layer of fluid may exert an upward pull.

One phenomenon of great interest in this connection has been shown (22, 23) in those animals whose spinal fluids are subjected, by laminectomy or by lumbar puncture, to the full pressure of the atmosphere when in the vertical head-down position. In both of these experimental preparations, maximum dislocation of the cerebrospinal fluid within the spinal subarachnoid space must be assumed. The occipital pressure in these cases increases approximately 185 mm. over the normal horizontal level of 125 mm.; the total pressure recorded is therefore slightly above 300 mm. in the occipital region. With air introduced in the lumbar needle, the fluid-level in manometer and spinal subarachnoid space must be taken to be the same; therefore under these conditions there is cerebrospinal fluid only sufficient to fill 300 mm. of the spinal subarachnoid space measuring 400 mm. in the dogs used. In the laminectomized animals similar conditions must hold except that the lumbar portion of the subarachnoid space undoubtedly still contains a capillary layer of

fluid. The identity of pressure-change in these two preparations demonstrates that this lumbar capillary layer does not exert any appreciable pressure downwards or upwards.

The application of these experimental findings to the general problem of pressure-conditions about the central nervous system of mammals which have assumed the semi-erect or erect posture for a considerable proportion of their daily life yields much in the way of suggestive hypothesis. It must be emphasized that the experimental data have been derived from anesthetized animals, and it is possible that the anesthesia itself markedly alters the character of the vasomotor response which has so strong a rôle in these positional pressure-alterations (23). On the other hand, such fragmentary data as we have from observations on human beings indicate the general application of the findings to unanesthetized mammals. Thus Barré and Schrapf (3), Zylberlast-Zand (31), Pfaundler (19), Ayer (2) and others have reported that the cerebrospinal fluid pressure at lumbar puncture is considerably higher when determined in the sitting than in the prone posture; most of the investigators record an increase in the neighborhood of 200 mm. of normal saline solution. Such an increase in man where the spinal length is approximately 600 mm. would fall in line with the pressure-decreases of the vertical tail-down positions in dog when measured in the occipital region.

Pfaundler (19) made use of the difference in pressure of the cerebrospinal fluid in children in the sitting and prone positions, to attempt an analysis of the factors responsible for the maintenance of the pressure. He considered the fluid's pressure to be dependent upon three factors: 1, elasticity of the meninges; 2, blood pressure; and 3, hydrostatic effects. Assuming that the prone position excluded the third factor, he determined the pressure of cerebrospinal fluid in the cadaver as a measure of meningeal elasticity, and arrived at the vascular factor by taking the differences. Pfaundler assigned definite figures to the three factors for the pressure of the cerebrospinal fluid for children (2 to 12 years) in the erect position: elastic, 8 per cent; vascular, 68 per cent; hydrostatic, 24 per cent. For the first year of life, somewhat different values were derived. While these analyses of the factors involved in the pressure of the cerebrospinal fluid are of importance, the determination of meningeal elasticity in the cadaver presents difficulties of accurate calculation, and the methods used were not adequate for the purpose. The studies indicate, however, great appreciation of the problem of hydrostatics in the erect posture of human beings.

A further clinical contribution to the hydrostatics of the problem has been made by Ayer (2) who reported measurement of the pressure in the cisterna magna of man in the erect posture; it was recorded as "below zero; i.e., it is a negative pressure." This finding is in accord with Walter's (20) conclusion, based on study of clinical cases with cranial defects, that in erect man the level of atmospheric pressure is in the mid-thoracic region; he has estimated that the pressure in the subarachnoid space in the vertex region would be minus 200–400 mm. (less than atmospheric) of salt solution. With this important deduction of Walter's the findings in the anesthetized animals unquestionably agree. Giving due consideration to the differences in spinal length in the various mammals, the projection of atmospheric levels from the menisci of manometers upon the animal's body in the two erect positions (head-down and tail-down) always falls within the animal's body, thus indicating that those portions of the subarachnoid space above the level of the projection are under pressures less than atmospheric.

Similar deductions are to be drawn from the experiments on cadavers carried out by Krönig and Gauss (15), though findings on cadavers must remain subject to grave criticism. With several manometers attached to needles in the subarachnoid space in the lumbar and thoracic regions, Krönig and Gauss found that the fluid-levels in the various manometers were all at the same height when the cadaver was placed in the sitting position; the menisci registered atmospheric pressure at the first or second thoracic spine. On exposing the meninges by laminectomy, fluid was found filling the subarachnoid space in the lumbar and thoracic regions, but no free fluid was noted in the cervical segments. These findings were confirmed by observations on a calf held in the vertical tail-down position: the lumbar needle registered a positive pressure while no fluid flowed from the needle in the lower cervical region. On bringing the calf to the horizontal position fluid escaped from this second needle.

These general assumptions derived from the experiments on animals, from clinical observations, and from the findings on cadavers, hold for the catarrhine monkey as well as for the four-footed mammals (cat, dog) whose normal posture is horizontal and whose heads are customarily carried at levels but slightly above that of the horizontal spinal cord. The macaque, while still exhibiting four-footed progression, lives as large a proportion of his life in the erect position as does man; the pressure-changes in the cerebrospinal fluid of the macaque on tilting are of the same relative magnitudes as are those of the cat and dog. The coefficient of elasticity of the monkey's intradural sac and

its contents is the same whether derived from head-down or tail-down tiltings; the fractions $\frac{dV}{dP}$ calculated from pressure-changes and volume-changes in the cerebrospinal fluid on the two tiltings are the same. One is inevitably led therefore to the conclusion that evolutionary progression which permitted the assumption of the erect posture by certain of the primates, was not accompanied by development of any specialized mechanism for the protection of the central nervous system against the hydrostatic pressures within the cerebrospinal fluid.

It may be advanced that the experimental data show some additional protection against positional change in the tiltings to the tail-down position (with head-up, erect posture) as the pressure-decreases recorded in the occipital manometer are less than the increases for the head-down position. This difference is not great (75 mm. as opposed to 105 mm. in intact animals of 400 mm. spinal length) and is to be largely related, in the interpretation ventured (22), to the inherent possibilities of inward collapse or expansibility of the spinal dural sac. Such protection as may be afforded by this character of the spinal dural envelope is possibly of constant magnitude throughout the mammalian class, but there are no observations permitting evaluation of the process as a protective agency.

If one accept the deduction that in the adoption of the erect posture in man there has been provided no especial mechanism for the protection of the central nervous system against changes in hydrostatic pressures in the cerebrospinal fluid, it becomes of interest to contemplate the pressure-conditions of the fluid in those mammals which exhibit extraordinary differences in the levels of head and spinal cord. It may be a matter of significance that all of the semi-erect and erect mammals have spinal lengths and head-heights which do not exceed those of man by any extraordinary degree; but in one four-footed mammal, the highly specialized giraffe, the head is carried at a level which in a full-grown male may measure 3 meters above the lumbar region. Information is of course lacking about subarachnoid pressures in this mammal but it is likely that in the horizontal position the pressure of the cerebrospinal fluid would be that of other mammals. In its normal posture with the head carried high in the air, one-fourth of the hydrostatic height of the 3 meter fluid column would be effective in the lumbar subarachnoid space, if the interpretation here ventured be correct. Such an assumption would make the lumbar pressure lie between 850 and 900 mm. of saline solution; atmospheric pressure would fall about the lower end of

the animal's neck, while at the vertex of the cranium a negative pressure up to minus 2200 mm. (less than atmospheric) would exist. The drinking habits of this mammal, depressing its head for only a few seconds at a time, may be related to the tremendous internal shift of cerebrospinal fluid which must occur in this positional change.

While the majority of the semi-erect and erect mammals apparently exist for a large proportion of their lives with intracranial pressures approaching zero or of negative values (less than atmospheric), other highly specialized mammals spend a great deal of the time suspended in the vertical head-down position. The largest of the fruit bats, the flying fox, affords the best example of this type: the resting and sleeping posture is vertical head-down so that the intracranial pressure is in excess of that of the horizontal position. But even the largest of these bats rarely has a spinal length over 400 mm., so that (applying the same method of reasoning) the intracranial pressures would range from 200 to 225 mm. of saline solution when the animal is suspended in its resting posture.

But such deductions or calculations rest upon very slight factual data except as it may seem possible to apply findings made on one mammal to others in this vertebrate class. It would seem as if the whole field of investigation is now but opening up for further, more fruitful studies. The need today is for additional information regarding pressure-changes in various mammals on tilting from the horizontal to the two vertical positions. Not only are further data required for those mammals whose habitual posture is horizontal, but also data are needed for those animals of the semi-erect series and for those whose habitual posture superimposes in extraordinary ways the hydrostatic column of the cerebrospinal fluid upon the normal pressures of the horizontal position. And there is need for more exact interpretation of the true meaning of the elasticity of the dural sac and its contents: why is the general coefficient of the system greater in younger animals than in older? Then too, what are the pressures within the cranium of man who spends two-thirds of his life in the erect posture: are these pressures less than atmospheric as the scattered data indicate? If so, why is there so much reference to cerebrospinal rhinorrhea with so little comment upon the possible change in intracranial pressures due to air in cerebral ventricles and subarachnoid space? And if this hypothesis of negative pressures within the cranium of semi-erect and erect mammals prove correct, how does it modify current theories of the production of cerebrospinal fluid by the choroid plexuses and of the processes of absorption? Will not all of our concepts

of production and absorption, as based on the four-footed mammal in its horizontal posture, now have to be reconsidered?

Yet even with all of these unanswered questions it seems fair to conclude that our knowledge of positional adjustments of the pressure of the cerebrospinal fluid has progressed since the time of Alexander Monro (18). His promulgation of a thesis to account for the functional workings within the cranium has stood in a way the test of time: reconstituted, modified, extended—the Monro-Kellie doctrine still must be looked upon as furnishing a basis for the possible interpretation of positional changes within the dural sac. With a known elastic element now introduced into the concept, it is possible to speak with accuracy of the fairly constant content of the cranial and spinal dural sacs—which after all is almost what Alexander Monro said one hundred and fifty years ago.

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CHRONIC EFFECTS OF EXERCISE

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This paper concerns itself with the more or less permanent changes in the organism, ascribable to exercise. In large part, these may be regarded as adaptations which facilitate the performance of more exercise. The sum total of these adaptations constitutes the "trained" state, which is attained by a period of "training." Whatever these changes are, their extent must bear a relation to the amount of training. Since in a mechanized society only sport remains to furnish common illustrations of maximum training, a picture as presented here tends to be one-sided. To what extent the permanent changes due to the more drab forms of exercise, called "work," coincide with those due to sport is not clear. There are sufficient "work" studies to indicate resemblances in the main lines. It will, however, be useful to remember that athletics consist of physical exercise plus more or less of emotional exercise, while work is likely to involve less and less of the emotions.

Though it is most important to distinguish between "Übung und Training" as the German literature puts it, it is unwise to contrast the terms. In this paper the development of skill or coördination as a result of practice is regarded as the lasting effect of training on the central nervous system. Since such an increase in skill means less internal work (measured by the oxygen requirement) for the accomplishing of a given task, less is actually required of, let us say, the muscular or circulo-respiratory system. Similarly the increase in alkali reserve, resulting from training, also lessens the load which the performance of a given task puts on the circulo-respiratory system. The point is that the resulting increased capacity for work should not be credited to improvements in the circulo-respiratory system, even though this system may most profoundly reflect the change. From another angle, there are illustrations indicating that until the circulo-respiratory system "learns" to perform sufficiently well, the body is unable to do enough work to call forth changes in some other organs.

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It is also conceivable that exercise may produce lasting changes which cannot be interpreted as facilitating further performance. Therefore this paper does not confine itself to the problem of training.

The advantages of discussing the literature under the anatomic systems seemed, to the author, to outweigh the accompanying undesirable necessity of repeated reference to papers which report on several systems.

MUSCULAR SYSTEM. *Muscle size, strength, and endurance.* Increases in muscle size, strength, and endurance are probably among the best recognized chronic effects of muscular exertion. The phenomena first found scientific generalization in the "aktivitätshypertrophie" and "inaktivitatsätrophie" theories of Roux (200). Careful studies in this field have shown that increases in *muscle girths* in consequence of their use, though demonstrable in children (Godin, 81), in youths (Matthias, 170; Herxheimer, 105), college students (Kohlrausch, 147), and adults (Herxheimer, 106), are not always proportional to the work done. Thus the findings of Matthias and Herxheimer indicate that during periods of rapid growth in body length, exercise had less effect on muscle growth than in periods when the tendency toward growth in diameter predominated. In his study of college students of physical education, Kohlrausch found that the thinnest "asthenic type" individuals responded least, whereas the middle sized showed greatest improvements in muscle girths. In his study of policemen in training, Herxheimer found greatest improvement in the underweight group. After a summer of track and field training Kohlrausch found reductions in muscle girths which had previously grown under the influence of heavy gymnastics, practiced in the winter months.

Bethe and Fischer (21) found in Olympic athletes the greatest *strength* in those muscle groups which the athlete employed most strenuously in his athletic specialty. Abramson (1) found that improvements in strength gained in a training period were still in evidence, though considerably reduced, a year later.

In a carefully controlled, long-term experiment Holck (125) found the *endurance* of his forearm flexors, measured on a Mosso type ergograph, continuing to improve in quite spasmodic fashion over several years; so that after four and one-half years he reached a high point equal to 500 per cent of the original endurance. Hedvall (98) reported an increase of 819 per cent in fifty days of training of the arms on the Johansson ergograph. He also found that within two months after the cessation of daily training, the work capacity of his legs had already fallen to one-third of the maximum attained in training.

The work of Siebert (217) has helped to throw light on the *nature* and *cause* of muscular hypertrophy. This investigator found the increase in gastrocnemius weight of rats a function of the speed of running rather than of the duration. Rats were exercised for a half year in motor driven drums. All ran the same distance but at various speeds. Hypertrophy was found in the leg muscles of the rats which ran at higher speeds. He found, also, that at a moderate speed, just enough to produce slight hypertrophy, conditions soon became stationary no matter how long the exercise continued and that further hypertrophy resulted only when the speed was markedly increased. Thus hypertrophy is a function of the amount of work performed in a unit of time. Kohlrausch (150) arrives at similar conclusions from observations employing his method of "in vivo" analysis of body components on dogs. In another series, Siebert stimulated daily for twenty minutes one leg of a frog to perform isotonic contractions while the leg on the opposite side was made to contract isometrically. After fourteen days of stimulation and two to three days of rest, the muscles were excised and weighed. The isometrically contracted ones averaged 13 per cent heavier than their isotonically contracted mates.

From most careful *histologic* studies of fibers in the sartorius muscle removed from one leg of each of two dogs before, and from the other leg after months of very strenuous running exercise, Morpurgo (177) found the increase in muscle mass due entirely to a true hypertrophy of individual fibers and not to the appearance of new fibers. There was no change in fiber length nor in the number of nuclei, nor the number or size of fibrilli in the muscle cell. Only the sarcoplasm was increased. The observations of Siebert (217) on the dog and Kleeberger (141) on the rabbit support these findings. The latter worker stimulated electrically the ear muscles of one side and observed increases of as high as 40 per cent in weight and 90 per cent in cross-section area, attributable entirely to enlargement of existing cells.

Belehradek (14) observed a *growth-stimulating* effect of tetanized muscle tissue when fed to tadpoles. Siebert and Petow (221) have completely verified these findings and Siebert (219) suggested choline as probably one of the active substances. He established also (218) (220) that the exercised muscle produced radiations active at a distance of 3 to 5 mm. in stimulating mitosis in onion root, and budding in yeast cultures. These workers, then, are seeking in some change associated with the metabolites or their oxidative removal (220), the adequate stimulus for hypertrophy of muscle.

Pigment. In rabbits and dogs, Günther (90) and Whipple (245) found pigment distribution in muscles to be proportional to their activity. Thus the heart and jaw muscles are best supplied in rabbits, and the leg muscles of a hunting dog contain two and one-half times as much as those of a quiet house dog. Whipple has identified this pigment as hemoglobin. Embden and Habs (59) report a marked increase in the amount of pigment in the biceps femoris of the rabbit after several weeks of daily faradization of its nerve.

Glycogen. By stimulating the leg muscle on one side while the other side remains as a control, Embden and Habs (59) demonstrated an increase in muscle glycogen which becomes apparent after five days, reaches its maximum in twelve days of stimulation and persists for at least five weeks after the end of this form of training. Palladin and Ferdmann (183) have confirmed this observation. Thörner (237) found higher glycogen percentages in the muscles of his trained dogs compared with controls from the same litter. By taping one hind leg loosely to the abdomen, Procter and Best (190) trained dogs to run on three legs. From comparisons of homologous muscles of the hind limbs of dogs killed after varying periods of this form of training, they found increasing amounts of glycogen in the trained muscles, during the first three weeks of training. In dogs killed after longer periods of training, the muscles of the active side gave values approximating those of the inactive side. Thus after thirty to forty days of training the two sides again have similar glycogen values. They conclude that an extra glycogen store is not essential in the trained state. The observations of Leese et al. (159) who found no relation between the glycogen content of the muscles of starving rats and their work capacity points in the same direction.

Phosphocreatin. A marked increase in the phosphocreatin content, which however lasts for only three to six days after cessation of daily electrical stimulation, was found by Palladin and Ferdmann (183) and Ferdmann and Feinschmidt (72) in the rabbit's biceps femoris.

Other changes. An increase in *potassium* which was noticeable, first, one to two days after cessation of training, and again disappeared within six days, was observed by Fomin (73) in rabbits' muscle stimulated unilaterally and in dogs exercised with one hind leg carrying an extra load to accentuate the training effects. The muscles on the weighted side yielded 17 per cent more of potassium than homologous muscles of the opposite side.

Employing the ability of a muscle hash to induce the *synthesis of*

hexose-diphosphate (lactacidogen) in a solution of 2 per cent $NaHCO_3$, 0.4 per cent glycogen and $\frac{M}{10}$ NaFl, as a measure of its enzyme potency, the Frankfurt workers (Embden and Jost, 60) have been able to show that a fatigued frog's muscle loses this property just as does a dying muscle, the difference being that in the fatigued muscle the loss is reversible by rest. The same has been shown by Milroy (176) for cat's muscle. From these and other points of similarity, Embden (58) has come to consider death and fatigue as comparable processes. Fatigue, then, is incipient death which is reversible. Habs (91) undertook to determine whether a trained muscle which is recognized as farther removed from the fatigue point, is also farther removed from death. He found that the muscle-hash of rabbit muscle "trained" by daily faradization, always retained this "*synthesefähigkeit*" considerably longer than its control from the opposite unstimulated leg. He found, also, that rigor mortis appears later in trained than untrained muscles. Corresponding with this finding, he was able to demonstrate also a slower appearance of inorganic phosphorus and of ammonia in the dying "trained" muscle.

Thörner (237) found a higher percentage of *water* in the muscles of trained dogs, while Embden and Habs (59), who compared muscle weights from the same animal, were able to show that the absolute dry-weight also always increased with training. This increase was partly in the acid-soluble nitrogen. Külbs (153) and Thörner report less fat content in the muscles of trained dogs.

These varied observations on altered muscle chemistry explain in part the greater ability of a trained muscle, and further efforts in this direction will no doubt continue to be profitable. The fact, however, cannot escape us that after all these factors and all improvements in oxygen transport and waste removal have been given their full share of credit, a large part of the improvement in strength and endurance of the trained muscle must be sought in perhaps more effective *innervation*, but certainly in improved *coördination* of the nervous impulses which from moment to moment must adjust muscle effort to the needs of the task.

Though one is inclined to view the factors measured in *viscosity* determinations by methods recently modified by Best and Partridge (20) as of the unchangeable endowments of an athlete, the alternative view that training may influence these factors has to the present author's knowledge not been ruled out by experiment. Whether the

respiratory ferment of muscle is in any way modified in the training process is still another question deserving of consideration as soon as methods become available. This is essentially the question raised by Bock et al. (see below) in connection with their observations on the famous Boston marathon runner, De Mar. Procter and Best, in their dog studies described above, found some evidence for the frequently advanced theory that trained muscles have an increased *buffering capacity* for acids. This question deserves further attention. The method employed by Atzler and Lehmann (7) for determining the "Pufferungspotenz" of tissues might be employed.

CIRCULATORY SYSTEM. *Heart size.* The questions which have faced workers in this field are these: Does an extended program of strenuous physical work or sport lead to a more or less persistent heart enlargement? If so, is this enlargement primarily a hypertrophy, i.e., an increase in the bulk of the myocardium with enlarged chamber capacity a secondary and natural concomitant, or is it primarily a dilatation, stretching, or greater relaxation of the heart wall with the consequent greater capacity responsible for the observed larger heart shadows? If there is cardiac hypertrophy, does it outweigh the hypertrophy simultaneously induced in the skeletal musculature? Other questions center around reversibility of the hypertrophy by rest, left or right-sided distribution, and signs of true heart injury.

In animals. The data from animal work are on the whole consistent. Bergmann (19), Parrot (184), Grober (86), and Hesse (120) showed that the heart-size of an animal reflects the amount of activity characteristic of its mode of life. Thus domesticated animals (19) have smaller ratios of heart to body-weight than their undomesticated relatives, and birds (184) who fly great distances or who fly clumsily with much wing action have unusually large hearts. Külbs (153) reports that the heart-weight of the wild rabbit after caging approaches that of the tame or hutch rabbit without a corresponding loss in skeletal musculature. Grober (86) found the hypertrophy in hares and wild rabbits, compared with hutch rabbits, to be markedly right-sided and attributed it to overstraining of the lungs in running from the enemy. Hiramatsu (121) was the first to find right-heart hypertrophy under experimental conditions. His rabbits were run long and strenuously and showed signs of acute emphysema. Herrmann (103) weighed the hearts of ten thoroughbred greyhounds and established heart-weight to body-weight ratios. Whereas two hundred normal mongrels averaged 7.98 grams of heart per kilogram of body with 9.98 as the maximum,

the most successful runner among his greyhounds had a ratio of 17.3. The average of 13.4 for this greyhound series exceeds that of the stag (11.5) which previously (19) held the highest average ratio observed for mammals. Herrmann concludes that the tendency to respond to exercise by hypertrophy is inherited in various degrees. In experimentally controlled studies Külbs (152), Grober (87), and Thörner (237), showed that the heart-weight to body-weight ratios of dogs exercised by running were markedly greater than those of their unexercised litter mates. Hatai (97), Secher (213), and Borovansky (27) reported similar observations on rats. The only contradictory findings are those of Bruns (31) who found skeletal and cardiac muscle hypertrophied to the same extent so that the ratios remained unchanged. His dogs were required to walk twice daily on a motor-driven tread-mill a distance of 2 to 3 km. forward and 1000 to 1400 m. uphill in one-half to three-fourths hour. This is an unusual speed and pitch to which further reference will be made. Secher (214) trained twenty-two rats by daily running in a drum for about sixty days. Then all were retired to inactivity and small groups killed at intervals to seventy-five days. In those killed immediately the heart-weight constituted 5 to 6 per cent of the body-weight. This percentage decreased until the forty-eighth day when it had receded to the normal values of 3.3 to 3.6 per cent. This is the first demonstration of the regression of experimentally induced exercise hypertrophy after training. Secher cites Dedichem as having observed reduction in the heart size of a ski champion after the season. In addition to the true hypertrophy shown by organ-weight, Thörner (237) observed by x-ray in his two exercised dogs, a more rapid increase of the long dimension of the heart and therefore an increased $\frac{\text{Length}}{\text{Width}}$ ratio. This finding, together with x-ray observations, interpreted as indicating a relaxed apex, he attributes to the increased vagus tone in trained dogs. Külbs (154) observed no hypertrophy in the hearts of dogs that were castrated or splenectomized before training. Though they ran as far as the normal dogs in his earlier series, these animals ran more leisurely. Failure in the castrate he attributes to a lack of "temperament," while for the splenectomy case he seeks a hormonal explanation. He cites figures from Bollinger indicating smaller hearts in the castrates of horses and cattle. Grober in the dog, and Borovansky in the rat, report greatest hypertrophy in the left ventricle. In the present writer's laboratory (229) (230) (231) the effects of running and swimming on the *growing* heart of dogs has

recently been studied in a series of eighteen puppies raised under controlled conditions. Roentgenograms were secured biweekly on exercised and control dogs throughout the period of observation (in most cases $1\frac{1}{2}$ years), and the results checked by post-mortem findings. We have been able to confirm the "hypertrophy" and "regression" findings of others, but could not detect changes in the shape of the heart as did Thörner. With one exception the hearts have hypertrophied uniformly, showing only slight left ventricle preponderance. The exercise effect makes itself noticeable in the growth curve of the heart within three to five weeks after the beginning of daily exercise. Differences in the amount of hypertrophy in various animals correlate fairly well with ability to swim and "desire" for voluntary running.

In man. In 1628 Harvey (95) said, "The more muscular and powerful men are, the firmer their flesh; the stronger, thicker, denser, and more fibrous their hearts, the thicker, closer, and stronger are the auricles and arteries." To Hirsch (122) most writers refer as having first demonstrated on the cadaver that the heart weight varies with the body musculature. His observations were made on fat, emaciated, and normal types. After Schieffer (205), and Dietlen and Moritz (49) had reported heart areas in habitual cyclists to be greater than in occasional cyclists or non-cyclists of the same corresponding size and age, Bruns (31) defines the issue in these words, "Gibt es bei gesunden Menschen eine Arbeitshypertrophie des Herzens, d. h. eine unverhältnissmässig starke Zunahme der Herzmasse durch Körperarbeit in Vergleich zur ebenfalls zunehmenden Skelettmuskulatur, oder besteht der Satz zu recht, dass bei gesunden Körperlich arbeitenden Menschen die Masse des Herzmuskels der Körpermuskulatur entspricht?" Students of this problem are today divided into three camps: first, those who say that the heart sizes of athletes and heavy workers fall within the range for normal individuals of the same size and age. Rautmann (193) (194) is regarded as spokesman for this group. The observations of Dibbelt (48) on heart-weights of soldiers killed in action, of Cohn (38) on returned soldiers studied by x-ray, of Podkaminsky (186) on a hundred heavy laborers, of Farrell et al. (69) on the American transcontinental runners, and Eyster (66) on athletes and coaches with long athletic records, are in support of this position. A second position taken by Deutsch and Kauf (46) and Deutsch (45) after examination of several thousand athletes of all kinds at the Vienna heart station and of thirty-two athletes at the 1928 Amsterdam Olympics, is that the heart shadow of trained athletes averages larger than that of similarly built individuals

who exercise for pleasure only. Oarsmen, skiers, and cyclists head the list with fencers, boxers, and football (American soccer) players merging at the lower end with the untrained. These observers believe that the psychic strain and excitement of certain sports contribute to this enlargement, and interpret the enlargement as a dilatation brought on by vagotonia in athletes. In the observation that the enlargement usually subsides (though never to the original) after weeks, and in the bradycardia of athletes, they find the main support for this interpretation which was originally developed by Schenk (203). The last named is of the opinion that even in cases where there is genuine hypertrophy the greater relaxation under vagus tone contributes its share to the total picture. In support of the third position, that of outright hypertrophy, Herxheimer is at once the greatest contributor and most forceful spokesman. This worker reported (107) (108) on 171 participants in the German games of 1922, (109) on 12 professional six-day bicycle racers, (112) on 3 athletes, and (115) on 249 Amsterdam Olympic athletes. Eimer's findings (57) on 300 academic athletes point in the same direction. Herxheimer presents his findings in terms of the heart coefficient, i.e.,

$$\frac{\text{Vol. of Heart}}{\text{Body Weight}}$$

where volume is calculated by the method of Nicolai and Zuntz (179), which assumes the heart-volume to be equivalent to that of a sphere whose radius is equal to one-half of the transverse dimension of the heart shadow. His findings (115) were as follows: Decathlon $\frac{1}{63.8}$; Sprinters $\frac{1}{62.3}$; Long distance swimmer $\frac{1}{60.8}$; Weight lifters $\frac{1}{56.8}$; Middle distance runners $\frac{1}{55.1}$; Short distance cyclists $\frac{1}{55.1}$; Boxers $\frac{1}{52.7}$; Oarsmen $\frac{1}{51.7}$; Long distance cyclists $\frac{1}{48.7}$; Marathon runners $\frac{1}{46.4}$. His 12 (109) six-day cyclists averaged $\frac{1}{40.3}$, the largest ratio on record. He presented the theory (110) that exercises of strength, speed, or big effort induce hypertrophy of the skeletal muscle and only to a small extent increase the heart mass, whereas exercises of endurance lead to heart hypertrophy whilst they leave the body muscles unchanged in size. This he says is the logical application of Weizsäcker's (244) principle, that the muscle which is taxed beyond its capacity is the one to respond with hypertrophy. (Siebert's observations on skeletal muscles cited above are virtually an experimental demonstration of this theory.) He emphasizes the importance of studying athletes with long records in single sports, preferably champions, to illustrate this law most clearly. Since

animals are usually exercised by "long distance" running which taxes the heart while leg muscles move comparatively slowly, this theory serves to generalize the consistent findings on animals as well as Brun's (31) exceptions. This worker, it will be recalled, caused his dogs to walk slowly on a highly pitched mill thus taxing the leg muscles and heart more equally. The issue between Herxheimer and Rautmann is sharply drawn in papers contributed by each to the same number of the Klinische Wochenschrift (114) (194). The position of both is weakened by the clinical nature of their material and the necessity of depending on various systems of norms and standards for the detection of changes in a heart shadow which in man is always partly fused with that of the diaphragm at its apical end. Ackermann (2) evaded the first of these difficulties by measuring hearts of the same oarsmen before and after a season of training. About half, mostly the younger men, showed definite enlargements at the end of the season. A number of veterans showed some reductions. He believes that his findings corroborate Herxheimer's position of hypertrophy in contrast to Deutsch and Kauf's "vagus dilatation." Recently Purjesz et al. (191) have made comparable observations on 54 men and boys while training in athletics and swimming. Their results, though not as convincing, point in the same direction. More studies of this nature on human beings are needed to clear the air. It appears to the present writer that the mass of evidence favors the view that in certain individuals, perhaps the majority, depending on constitutional type, exercises of the endurance form will induce a growth of heart muscle in excess of contemporary changes in skeletal muscles. This hypertrophy is probably bilateral, is more likely to occur in the young, will regress at least in part with the cessation of training, and is very likely an asset to the individual in the pursuit of his sport. With this hypertrophy there may or may not also be a relaxed apex and heart wall (112) (63) (not pathological dilatation) associated with the longer diastole of the vagotonic bradycardia. There is no reason to assume that this hypertrophy is in any sense a response to injury of the kind described by Eyster (65). It seems more logical to class it with other temporary functional hypertrophies such as Secher (215) found in consequence of administration of frequent doses of adrenalin to rats, and Jensen and Norgaard (130) found in the later months of human pregnancy. Good reviews of the literature are found in (31) (46) (186) and (116).

Pulse rate. It is generally conceded that trained athletes have low resting pulse rates. The literature is full of single observations gathered

in clinical fashion from persons with athletic careers. Illustrative of these is the report of Hoogerwerf (127) on the Amsterdam Olympic contestants. The average rate of the 198 he examined was 50. Many had rates as low as 40 and some even 30 per minute. The counts were taken from electrocardiograms. On 202 athletes of this same Olympiad, Bramwell and Ellis (28) found 66, 63, 61, and 58 as the average heart rate for sprinters, middle distance, long distance, and marathon runners, respectively. The average ages were 22, 23, 24, 27, in the same order. Weight lifters, with an average of 25.7 years, averaged 80 beats per minute. Of greater value are observations on the same individuals before and after a period of training. Reductions in pulse rate under such conditions are reported by Lindhard (165) for one bicyclist, in a season of training, Dawson (43) for himself in several seasons, Herxheimer (111) for eleven policemen in eight weeks' training, Kaup and Grosse (138) for nine subjects in two months' training, Schneider et al. (207) for five subjects in at least two months with daily moderate exercise. Ackermann (2) found reductions in 65 per cent of experienced oarsmen and 58 per cent of first year men in a season of training in rowing. He finds the decrease mostly in those whose hearts also enlarged. Gemmill, Booth and Pocock (78) observed no significant changes in the *basal* heart rate of three subjects trained to light work on a bicycle ergometer. The present author in unpublished studies also did not regularly find reductions in the *basal* heart rate to follow a period of training in dogs. The possibility that the rate under strictly basal conditions is not subject to change by training as is the rate in resting (usually sitting) position which itself requires some exertion, deserves further consideration. Herxheimer (111) (116) finds that training has less effect on the rate in younger individuals. Practically all of these workers and in addition (212) (80) (101) (23) report that the trained heart accelerates less in exercise or when merely the upright position is assumed. Kauf (137) found that in contrast to untrained individuals the hearts of trained athletes failed to accelerate after 1 mgm. atropine. Since adrenaline in the customary dosage accelerated these hearts, Kauf is led to conclude that the training effect is due to an increased vagus activity. These observations should be verified since Herxheimer (104) found negative results with atropine under comparable conditions.

Cardiac output. All observers are agreed that in rest the trained or athletic subject has a higher minute-volume than the untrained. Lindhard (165) employing the N_2O method of Krogh and Lindhard re-

ported that a period of training increased the resting minute-volume of the same individual by about 20 per cent. Thus the trained individual has a low coefficient of oxygen utilization *at rest* and may be said to have a relatively uneconomical circulatory adjustment. Since the trained state is also accompanied by a distinctly slower pulse, it is obvious from the formula: Minute-volume = Rate × Stroke-volume, that the stroke-volume is much larger in the athlete. Thus the runner, DeMar, (23) had a resting stroke-volume of 120 cc. which was 50 to 100 per cent greater than that of the three non-athletes in the series.

Concerning the effect of training on the minute-volume determined *during work* there is not the same unanimity of opinion among observers. A chart prepared by Hansen (92), combining data from nine different workers, is a surprising argument for the existence in general of a linear relationship between cardiac output and oxygen consumption ranging from 200 to over 4000 ccm. per minute. Such a relationship bespeaks a constant coefficient of oxygen-utilization or A-V difference which apparently does not hold for the same individual at all work-levels or in various stages of training. Thus Lindhard (165) and Collet and Liljestrand (39) found higher oxygen utilization and correspondingly lower minute-volumes for a given oxygen consumption, after training. With the acetylene method, Christensen (36) has found similar though less pronounced differences. This worker who, by the way, has observed minute-volumes up to 37.2 liters (the highest on record) at work levels requiring 3.9 liters oxygen per minute in the "steady state," found increasing oxygen-utilization in a given subject, up to a certain work-level beyond which the utilization again dropped. With training this oxygen-utilization increased at each level and the minute-volume decreased accordingly. This circulatory economy, as it is called, is attributed by these workers to better peripheral "regulation" which forces a larger fraction of the circulating blood through the working muscles. Grollman (88) finds in the more economical use of muscles after practice and the consequent diminished return of venous blood to the heart, a partial explanation of the difference. The excessively high exercise minute-volumes found in certain types of cardiacs are attributed by Eppinger et al. (61) to undue peripheral dilatation in the absence of sufficient acid-buffering ability, and compared by them with the "untrained" state. Lindhard and Christensen favor the view that a declining oxygen-utilization indicates that the individual is reaching the limits of his work capacity. It should be mentioned that the author of the acetylene method has repeatedly (12), (89) warned against its use in

work experiments with high minute-volumes. On this basis he challenges the findings of Christensen, who has, however, (34) (37) ably defended his position in applying the method to exercise studies. In contrast, Bock et al. (23) (9, p. 184) hold that in trained subjects the minute-volume for a given oxygen consumption is higher than in the untrained. Their position is based on a comparison of different individuals representing various stages of training, whereas the Copenhagen workers have observed the same individuals before and after training. It should further be noted that Bock and co-workers used a method based on the Fick principle which involves securing estimates of the CO_2 content of mixed venous blood from analysis of respiratory samples. More observations are necessary to settle the question.

Eppinger et al. (61), Ewig (62), Henderson et al. (101), and Bansi and Groscurth (10) conclude that the exercise increase of minute-volume in the untrained is brought about almost entirely by increases in heart rate, whereas the trained subject accomplishes the same more economically by increasing the stroke-volume more extensively. Though their trained subject always maintained, by far, the highest absolute stroke-volume, Bock et al. (23) found greater increases, compared with resting values, in their untrained individuals than in the trained.

From studies in which persons were trained to perform successively heavier work on a bicycle ergometer, Christensen (35) (36) found a new adjustment of the heart rate and stroke-volume at each level. If after these reached a constant value for a given load, the subject again returned to a lighter load, there was less acceleration of pulse and a larger stroke-volume than when this task had been performed before. Thus working with an "overload" adjusted the heart to perform more economically at the lower level than training at this level, no matter how long continued, was able to bring about. An extension of this principle would account also for the slower pulse and larger stroke-volumes of trained individuals at rest (104) (62). The observation further illustrates that the heart muscle responds to overload as does skeletal muscle, in accord with Weizsäcker's principle of hypertrophy.

The contentions of Bohnenkamp and co-workers (25) (26) that in the frog's heart the energy expenditure, oxygen requirement per heart beat, and the rate of fatigue, are functions of the heart rate no matter how large or small the stroke-volume, indicate the nature of the economies effected by increasing stroke-volume instead of rate.

Bansi and Groscurth (10) find in the smoothness with which the curve, representing minute-volume after exercise, returns to normal, a measure

of the degree of training. And Turner (239) reports that only the most "fit" women are able to stand quietly without reduction in minute-volume.

Changes within the cardiac cycle—electrocardiogram. In highly trained athletes, Hoogerwerf (127) and Csinády (41) found very long P – Q intervals in grams secured at rest. Thörner (237) found this interval lengthened in controlled experiments on two exercised dogs. In the present author's laboratory, this was not found as an invariable consequence of training. The possibility of the P – Q interval remaining unchanged in spite of an increased vagus tone is discussed in the paper presenting these findings (228). Takahashi et al. (234) have reported differences in the behavior of the time values of P – Q and Q – T in trained and untrained individuals following strenuous exercise. From comparisons of the actual value of these intervals with predicted values calculated from the formulae: $P - Q = 4.7578\ (P - P)^{0.275}$ (Takahashi) and $Q - T = 8.33\ \sqrt[3]{P - P}$ (Fredericia), these workers found that in trained individuals the values after exhausting exercise approximated fairly closely the predicted values, whereas in untrained individuals they deviated more in the direction of lower values. Such a condition could probably be best explained as due to greater sympathetic nerve activity in the untrained. Unfortunately their group of 100 examinees contains only four untrained subjects.

There is a young, but growing literature reporting the effect of training on the contour of the electrocardiogram. Unfortunately little of it represents controlled studies. The following observations have been reported. The P wave is low (127) (237) in trained subjects at rest and increases as a result of work (234) (127) (151). The S wave in rest disappears with training (237) and increases in exercise (234). The resting T wave, according to all of these workers, is increased by training. Following work, the T wave of a "fit" heart is unchanged or further increased (127) (151) (196). Hoogerwerf (127) and Csinády (41) each report U waves in two athletes with exceptional records. Only Thörner made observations on the same individuals (dogs) before and after training. In the author's own study (228), electrocardiograms were secured at rest from a total of nineteen dogs at biweekly intervals throughout inactive and training periods. From this large body of data it was found impossible to make any generalizations concerning characteristics in the form of the electrocardiogram attributable to training. Repeatedly the "picture" of training, described by others, was found in untrained dogs.

Blood pressure. Though Dawson (43), Schneider et al. (207), and Gemmill et al. (78), report no significant changes in resting blood pressure due to a training period, it must be recognized that in all these cases the exercise was comparatively mild or the training period of short duration. From studies on groups undergoing a much more strenuous program the results are different. Thus Wyman (250), Herxheimer (111) (113), Ewig (62), and Ackermann (2) found, in a majority of cases, considerable reduction in the resting *systolic* blood pressure in consequence of strenuous training. Herxheimer finds that this drop (in the average case, from 116 to 106 mm. Hg) is not observable until after the strenuous daily practice of a training period gives way to more moderate daily exertion as training is rounded out.

Both Ackermann and Herxheimer found the decrease less noticeable in youthful athletes or in the first year of training. In fact, they report some increases in such groups. It is likely that the occasional rises which Purjesz et al. (191) observed in a group of men and boys in training are in the same class.

Damez et al. (42) found larger *pulse pressures* in "athletic" girls compared with non-athletes. Herxheimer (111) found an average pulse pressure of 39.5 mm. Hg in a group of 35 record athletes. Ackermann reports a drop in *diastolic* pressure in 88 per cent of his subjects. Bramwell and Ellis (28) found 90 mm. Hg as the average diastolic pressure of Olympic weight-lifters while the runners averaged 75 mm.

It is generally considered a sign of fitness if the systolic pressure remains unchanged or rises slightly while changing from a lying to a standing position. A number of "fitness" tests such as Crampton's and Schneider's include this factor. Though Scott (212) found an improvement in this direction in ten out of twelve men whom he observed in a training period, it is a common experience among all who have employed these tests that in many excellent athletes the systolic pressure is lower in the upright position. Turner (239) (240) presents evidence that the "unfit" woman is marked by a *progressively falling* pressure, as quiet standing is continued for fifteen minutes.

Blood pressure reactions to exercise. In this connection, Dawson (44, p. 459) summarizes as follows: "(a) The systolic pressure rises more rapidly and much higher than is the case on the untrained individual; (b) the diastolic pressure often returns to normal before the cessation of the exercise; (c) the pulse pressure is enormously increased. Before training, the rise in pulse-pressure was from 38 (normal) to 62, after training from 37 to 114; (d) the product P.R. $\times$ P.P. is also greatly

increased (before training the rise was from 2660 (normal) to 6820, after training from 2220 to 12540). . . . ." Fabre (67) reports similar findings and emphasizes a rapidly falling systolic and more slowly falling diastolic, shortly after the beginning of work, as marking the untrained. Lampert (156) found in untrained skiers similar conditions which, however, disappeared after two weeks of training. Eppinger et al. (61a) found that the inability of cardiac cases to do even a mild amount of work was associated with an almost immediate appearance of lactic acid in the blood resulting in great peripheral dilatation. They assume a very low buffering power of the muscle cell as responsible for the phenomenon. The likelihood of this explanation applying to the question here considered ought to be investigated. In the highly trained runner, DeMar, Bock et al. (23) found no marked increase in systolic pressure until work equivalent to 2000 cc. O_2 per minute was performed, while in their untrained subjects very marked rises appeared with smaller loads. They believe that, "a varying elastic response of the aorta in different subjects may be a factor of great importance with reference to systolic pressure, resistance being related to the manner in which the aorta accepts the load discharged with each systole," and conceive that this function develops with use in the athlete.

Blood. *Erythrocytes.* There is no agreement as to whether a period of training produces a lasting change in the number of red corpuscles. The current belief that training induces a gradual increase in the per cent of hemoglobin, the total mass of corpuscles, and the total volume of blood, rests on but meagre experimental data. Isolated observations, such as Herxheimer (116, p. 719) reports from a forty-four year old former champion cyclist with a count of 7,120,000 erythrocytes are of no great significance in themselves. Schneider and Havens (209) observed three individuals throughout a period of training. Two showed increases of 3.6 and 9.4 per cent in Hb and erythrocytes, while a third showed no change. Volume studies which were performed on the one who showed the smaller increase indicated no change in blood volume throughout this period. Ackermann and Lebrecht (3) report a number of veteran oarsmen with erythrocyte counts over six million before the training season. But the majority of veterans and first year team men showed reductions in the number of red cells at the end of the season. Of the veterans, 82 per cent showed an increase in hemoglobin at the close of the season, while among the new men, 78 per cent showed a decrease. Ewig (63) found in some subjects a slight increase in hemoglobin due to training. Thörner (236) reports erythrocyte

counts of 5,360,000 on eight untrained students at Bonn, 5,000,000 for eight trained students, and 5,240,000 for forty-two Amsterdam Olympic athletes. He also reports values of 29.5×10^{-12} g., 28.3×10^{-12} g., and 27.7×10^{-12} g. for hemoglobin content per corpuscle, for the groups listed in the same order; 30.0×10^{-12} g. is the normal hemoglobin content of a corpuscle, according to Bürker. Thus Thörner observes lower hemoglobin values among trained athletes, while the corpuscle count is practically that of the normal individual. Thörner (238) found comparable reductions in erythrocytes and hemoglobin in trained dogs compared with untrained littermates. Also pointing to a comparative scarcity of iron in the trained state is Külbs' (154) observation of greater stores of iron in unexercised dogs than in littermates who were trained.

From total cell-volume, hematocrit plasma-cell volume ratios, hemoglobin percentage, and red corpuscle counts on a series of dogs, in and out of training, Broun (29) (30) is led to the conclusion that, whereas strenuous exercise causes destruction of red corpuscles, this reduction is only temporary and related to the extent of the previous inactivity. In some dogs, not all, he found as an after-effect, a genuine plethora in which the erythrocytes participated. The reports of Gurejew (90a) also on dogs, though not including total volume determinations, support Broun's position. These findings explain the increased osmotic resistance of red corpuscles observed by Thörner (236) (238) in trained athletes and dogs as due to a "weeding-out" of the older and less resistant corpuscles by the process of fragmentation which becomes accentuated in the high circulatory rates of exercise. The *in vivo* hemolyses and consequent increased resistances of surviving corpuscles observed by Hastings (96) point in the same direction. Külbs (153) and the present author (229) found that with but few exceptions the bone-marrow of exercised dogs is markedly redder than that of their unexercised littermates. Of increased bone-marrow activity in exercise there is no doubt. *The question remains whether this increased activity outlasts the actual exercise period sufficiently long to induce a polycythemia.* Thörner points out that the polycythemias observed in high altitudes are not accompanied by an increased corpuscle resistance. If one attempts to bring these exercise and altitude phenomena to a common denominator by accepting anoxemia as the stimulus to the bone-marrow, then it is probably more correct to assume the anoxemic condition consequent upon the destruction of the more fragile, older corpuscles early in the training period (in Broun's dogs as high as 20 per cent of the total blood) as this stimulus, rather than the increased O_2 consumption of the

tissues in exercise as Herxheimer (116) suggests, since in the most strenuous exercise periods there is no marked reduction in arterial O_2 and the venous return from muscles cannot influence the bone-marrow. An anoxemia-stimulus based on an anemia would cease to operate as soon as the normal number of corpuscles, or better, oxygen capacity was restored. Thörner (238) observed not only reductions in hemoglobin attributable to training, but also a reduction in erythrocyte diameter (7.30μ in the trained as compared to 7.50μ in the untrained). Though the significance of this is not clear, it should be viewed in the light of a recent study by Leichsenring and Hönig (162) who found that after massive bleeding of dogs the total cell volume (hematocrit) remained at a constant and low level for the succeeding twelve weeks. In the meantime, the corpuscle count slowly rose to equal and exceed the original values. Conversely the red cell diameter and calculated individual cell volume dropped continuously just enough to keep the total cell volume constant.

There is need for an extended investigation of this entire problem on man. Such a study must measure the total erythrocyte mass so that the possibility of storage phenomena and possible changes in these, induced by training, can be ruled out or evaluated. (The recent observations of Gurejew (90a) on dogs indicate no change occurring in the storage mechanisms.) It should also attempt to determine whether, with proper food, light, etc., exercise is able to stimulate the production of increased amounts of the essential corpuscle "stuff" or whether it merely hastens a turn-over process in which the material of red corpuscles more quickly becomes available for the manufacture of new ones.

Leucocytes. The few scattered observations on the *total* leucocyte count in the trained state which are reviewed by Thörner (236), though suggesting a slight leucocytosis, are in fact inconclusive. Whether the solution of this question can be attained by more careful observations in the *completely basal state*, emphasized by Garrey and Butler (76), or whether we shall have to await some more definite method of determining the total white corpuscle content of the body is, as yet, not clear. The latter seems the more probable.

Concerning changes in the *differential count* or the relative leucocyte picture there is considerable unanimity. Herxheimer (111) reported a relative *lymphocytosis* in highly trained individuals. He reports an average of 37 per cent of this type. This has since been verified by Ackermann and Lebrecht (3), Schulz (211), and Thörner (236). Correspondingly there is a reduction in the number of neutrophiles at the

expense of the older, segmented forms. This movement of the blood picture "to the left" was first observed by Egoroff (55) as an acute effect of exercise and has been described by Thörner as a "hold over" effect in well-trained athletes indicating in the white picture a condition of youthfulness analogous to the increased osmotic resistance observed in erythrocytes. Schulz observed also a reduction in *monocytes* from 6.6 to 2.0 per cent. Thörner did not find this change. The latter worker observed a distinct increase in the percentage of *eosinophiles*, particularly in his dog experiments. Egoroff et al. (56) who have studied this field extensively, find that with the attainment of the trained state there is less and less distortion of the white blood picture in consequence of a single bout of exercise. Thörner found the *lymphocytosis* best developed in the marathon runners and believes that there is some evidence that it is a mark of good condition. Of its etiology nothing is known. Thörner sees in it another manifestation of parasympathetic tone. Schulz found that it disappeared after two to four weeks of rest.

Thrombocytes. Behrens (13) reports an increase in the number of blood platelets in trained athletes who therefore show less further increase in this element in the acute response to exercise.

Alkali reserve. Following upon Herxheimer's (111) observation that a period of training increases the alveolar CO_2 tension, Walinski (243) found an average increase of 10 per cent in the alkali reserve (Van Slyke method) of five soldiers in a three months' training period, and Wissing (248), and again Full and Herxheimer (75) reported an average of 72.12 cc. CO_2 per 100 cc. in thirteen highly trained athletes as compared with an average of 65.15 cc. for twenty-two untrained normal individuals. In moderately trained athletes no change was observed. Rehberg and Wisseman (195) confirmed these findings on soldiers whom they followed through a training period and observed further that with continued, excessively heavy training there was ultimately a secondary reduction which they attribute to "overtraining." Ewig (64) observed both increases in the alkali reserve and the alveolar CO_2 tension as a result of a training period. He considers this as a form of overcompensation or "chemical training" in response to the acidosis of exercise. Unpublished findings of the present author, confirmed by Thörner (238), namely, that a period of training produces *no change* in the CO_2 content of *dogs'* blood, await repetition in the light of findings reported by Rice and Steinhaus (197), which indicate that during tread-mill running dogs' blood tends to become *alkaline* rather than acid, due to the "blowing off" of CO_2 in panting. To determine the possible rôle of acid

in evoking the higher alkali reserve observed in man, it will be most instructive to repeat the study on dogs trained by swimming in water at 15 to 25°C., since this form of exercise is accompanied (197) by blood changes toward the acid side as regularly found in man while exercising. It is the author's opinion that *this difference between the response of dog and man must be recognized in the interpretation of all exercise experiments employing dogs*, and by proper experimental manipulation may contribute to the solution of a number of exercise problems.

Blood sugar. There are no observations which indicate a change in the resting blood-sugar level induced by training. That training results in less and less fluctuation of the blood-sugar level during strenuous exercise is indicated by the work of Levine et al. (163) who observed a relation between the blood-sugar level and fitness in eleven marathon runners at the finish of a race; by Hoffman (124) who observed first a disappearance of the initial hyperglycemia and, as training progressed, a disappearance of the terminal hypoglycemia of exercise; by Deutsch and Weiss (47) who found hypoglycemia after a 10,000 meter run only in the least trained, and by Matthies (171), and Kestner et al. (139), who report much smaller reductions of the blood sugar level in consequence of three to four hours of gruelling physical exertion after a period of training. That the terminal hypoglycemia at times as low as 0.042 per cent observed by the latter workers is due to an exhaustion of sugar stores seems to follow from Wakabayashi's (242) glycogen determinations of the livers of trained and untrained rats after exercise, but whether the difference between the trained and untrained response is due to greater glycogen stores in the trained muscles (59), whether the increased muscular efficiency seated in better coördination results in more economical usage of the available supply of sugar, or whether with training there develop greater facilities for converting proteins and perhaps fats into sugar, remains as yet unsettled. The second of these positions is the simplest and should be ruled out before more complicated theories are set up. It should be recalled also that not all observers have found a relation between muscle glycogen and training. Leese et al. (159) found no connection between liver glycogen content and the work capacity of rats' leg muscles. Their form of exercise (galvanic stimulation) was, however, not entirely natural.

Other changes. Burge (32) reports increases in the *catalase* content of the blood in consequence of a season's football training. Schenk (203) reports increases in the *potassium* of the blood of trained persons, but Ewig (64) could not verify this finding. Harvard and Rea (94)

found that a period of exercise produces less reduction in the blood *phosphate* of trained than of untrained man. Kácl (135) found the increases in blood *creatin* and *creatinin* brought on by a bout of exercise, to be markedly smaller in trained than in untrained individuals. His observed changes are all very small (less than 1.0 mgm. per cent).

Huntemüller (128) for man, and his assistant, Dobrowolny (52), for rats, report increases in the *alexin* (complement) titer accompanying the trained state. Both report regular reductions in this titer when trained individuals are exercised to exhaustion. Untrained men and rats, they say, reach the point of exhaustion too soon so that their alexin titer is not endangered. The extent to which the alexin titer is a measure of resistance to disease is questioned by many immunologists. Goldner et al. (83) found a reduction in the complement titer of blood following brief periods of exercise, but could relate it in no way to the degree of training. Jokl (132) (133) (134), with refined methods, studied separately the variations in *amboceptor* and *complement* titer of many individuals before and after exertion. He found that these values fluctuated considerably in the same individual, that both were usually increased after short or long periods of exercise, and that there was absolutely no correlation between the degree of training and the observed values.

The "*critical level*" (Owles, 182), marking the appearance of lactic acid in the blood of an individual at work and the reciprocal reduction of the total blood CO_2, varies according to Bock et al. (23), Talbot et al. (235), and Dill et al. (50), with the individual and the degree of training. That this is only in part related to the greater efficiency coincident with improvement in coördination (skill) is evident from their observations in which the work done was measured and compared in terms of O_2 consumption. The work of Schneider and Ring (210), which shows that with training there is an increase in the "crest load," i.e., the maximum amount of work which can be performed before the alveolar CO_2 tension begins to drop, points in the same direction. Correspondingly, Bock et al. report the magnitude of pH distortion toward the acid side related inversely to the degree of training. The latter group of workers cannot see in improved circulation and respiration, alone, the complete answer to the remarkable efficiency of De Mar who was able to consume 3,500 cc. O_2 per minute at the end of a fifteen mile run before breakfast, without appreciable changes in blood CO_2 or lactic acid, while others showed marked changes at performance levels of one-third to one-half this magnitude. They therefore speculate, "we believe changes in the oxidation to be the most striking compensatory adjustment established

by training." Ewig (64) found some indications for an increase in serum proteins induced by training. Dill et al. (50) studied the changes in blood concentration during a bout of exercise but could find no differences which could be associated with the trained state.

Lindhard (165) and Christensen (36) are inclined to view an increased coefficient of oxygen utilization during work as a mark of the trained state. This they attribute to a better vasomotor regulation which permits less blood to pass through inactive tissue. This position is not inconsistent with the observations on blood pressure changes during exercise in trained and untrained individuals.

RESPIRATORY SYSTEM. *Lung weight.* Both Külbs (153) and Thörner (237) found that the lungs in exercised dogs represented a higher percentage of the body weight than in unexercised litter mates. Steinhaus et al. (229) were unable to confirm these observations in a similar study on very young growing dogs. These workers found that, whereas running exercise induced no significant change, dogs exercised by enforced swimming had noticeably *lighter* lungs than their controls. It would appear that further studies designed to answer this question are desirable.

Vital capacity. There is agreement among workers that training is accompanied by increases in vital capacity. Thus from records of 4000 athletes, Worringen (249) found average capacities of 3950 cc., 4300 cc., 4750 cc., and 5450 cc. in weight lifters, soccer players, track men, and oarsmen, as compared with 3250 cc. for non-athletes. His table contains a more complete list. White and McGuire (246) found moderate increases of about 5 per cent during a period of training in a citizens' military training camp. Wachholder (241) also observed differences in athletes of various sport types and observed an average increase of 650 cc. among oarsmen in a season. As is to be expected, such increases come only in novices. Thus Herxheimer (116, p. 727) found none during the training of seasoned oarsmen. There is danger of over-emphasizing vital capacity as a measure of fitness. Wachholder reports exceptional athletes with very low capacities and poorly conditioned subjects with figures comparable to the best athlete. The view expressed by Worringen that impending "staleness" or overtraining signals its advent by reductions in vital capacity has been denied by Herxheimer (116, p. 728). Schmith (206) agrees that in overtraining vital capacity is reduced, but refutes its predictive value. From his examination of a large group of heavy laborers only 5 per cent of which showed signs of emphysema, Podkaminsky (187) concludes that heavy exercise cannot be considered a primary cause of this condition.

Respiration at rest. Whereas Hoernicke (123), Knoll (142), and Ackermann (2) report slower and more even, deeper, resting respiration, as characteristic of trained individuals, Schneider et al. (207) and Gemmill et al. (78) found no such change in subjects whom they observed before and after training. All of these observers are agreed that there is no change in the minute-volume of the resting ventilation.

Kohlrausch (145) found that well advanced back-stroke swimmers exhibited a type of costal breathing in which the greatest mobility of the ribs is observed in their dorsal portions. He calls this the "back" type of thoracic breathing and claims that it gives the back-stroker the advantage of a more submerged "air-cushion." In contrast he finds the breast-stroker exhibiting the "front" type of thoracic respiration. In long distance runners he also finds the "back" type which he believes in this case to be due to the extensive arm action tending to immobilize the chest. It is surprising that a report of so interesting an adaptation has found neither verification nor denial in the decade since its appearance.

The traditional view that men breathe abdominally whereas women, excluding savages, breathe thoracically, though held untenable today, has recently been scrutinized from a new angle. Okuneva et al. (180), upon observing that Russian women in industry were largely abdominal breathers while girl students were not, sought to relate this to the occupational differences of the two groups. They found that girl students held their breath when lifting a 20 kgm. weight while the women in industry continued to breathe. When they trained sixteen costal-breathing girl students by daily lifting of such weights, they all became abdominal breathers within six weeks. Thus they conclude that the "male" type of breathing is an adaptation to permit activities requiring a rigid thorax without interference with respiration. These observations raise the question whether modern woman's return to abdominal breathing is due more to her having approximated savage woman in dress, as is usually taught, or in occupation.

Respiration in exertion. The commonplace that training results in economical ventilation during work has been repeatedly verified. Gemmill et al. (77) characterize the decrease in total ventilation during their standard exercise as the most marked change attributable to training. Gottstein (84) reports that training induces deeper, and therefore, slower breathing during work. Kagan and Kaplan (136) emphasize the more rapid return to normal after work. So that improvements in skill with their accompanying reduction in work cost

should not becloud measurements in this field, Simonson (223) adopted the K. V. Q., "Kalorischen Ventilationsquotienten," as a more accurate measure of respiratory efficiency. Thus his

$$\text{"resting K. V. Q."} = \frac{\text{Resting Resp. volume (in cc.)}}{\text{Resting Metabolism (in Cal.)}}$$

and the

$$\text{"work K. V. Q."} = \frac{\text{Total ventilation volume} - \text{Resting ventilation volume (in cc.)}}{\text{Total metabolism} - \text{Resting metabolism (in Cal.)}}$$

All respiratory volume measurements are reduced to standard conditions. The percentage relation which the work K. V. Q. bears to the resting K. V. Q. becomes a simple way of expressing the respiratory response to work. Expressed in this way he found reductions from 57.0 to 29.1 per cent and from 57.5 to 22.0 per cent due to training, when the test work was heavy; and from 38.3 to 19.4 per cent and from 15.2 to 1.0 per cent in the case of lighter work. Without doubt these differences reflect reductions in the appearance of lactic acid in the blood in consequence of improved oxygen transport in the trained state.

The theory of Magne (169) that the *respiratory center* develops a decreased irritability to acid has recently also been espoused by Herxheimer and Kost (117) to explain the increased resting alveolar CO_2 tensions in trained individuals. Its general acceptance, however, must await decisive experimental demonstration. It is clear that an increase in alkali reserve as reported for the trained state by a number of workers (see above), would operate to produce changes of the same kind.

METABOLISM. *Basal metabolism.* For a critical analysis of the literature on this subject the reader is referred to earlier writings by the author (227) (230). It will be considered sufficient to render here a brief summary of the trends in this field. Previous to 1925, at least seven authors (253) (252) (18) (165) (167) (129) (168) reported increases in basal metabolism in the trained state. Only Benedict and Carpenter (16) reported lower basal rates in athletes than non-athletes, but they questioned their own findings and Benedict and Smith (18) were led to refute this position. Since 1925, twelve papers (226) (207) (227) (17) (158) (85) (204) (78) (174) (230) (22) (208) have reported that a period of training either is without effect on the metabolism or that it lowers it very slightly. During the same period only three papers (155) (68) (199) report rises due to training. Of this group, Szakall, a co-author with Farkas (68), has more recently (personal communication) made

observations indicating no increase. In the light of our present knowledge it appears clear that the workers who have reported increases in basal metabolism have committed one or more of the following errors: 1. Failure to rule out the possibility of "after-effects." Very strenuous work, or moderate work in very flabby, heavy subjects may produce soreness or other yet unknown changes which exhibit themselves in raised metabolism for even longer than twenty-four hours. The works of Herxheimer et al. (119), Radtke (192), Wishart (247), and Schenk and Stähler (204), throw light in this direction. 2. Failure to observe conditions necessary to secure basal values. 3. Compared athletes with standard values later shown to be unsound. 4. Failure to rule out the spontaneous changes in basal metabolism which, according to Benedict (15) and Wishart (247) as well as others, play over a range of ± 15 per cent of the average figures for the individual. 5. Failure to conduct the tests in and out of training under identical conditions of rest, starvation, etc. 6. Failure to control the diet in and out of training. The tendency, sometimes observed, for basal metabolism to be slightly lower in consequence of training has been attributed by Steinhaus (227), Schenk and Stähler (204), and Schneider and Foster (208), to the improved ability to relax, accompanying the greater "muscle awareness" developed in training. That it may at times be due to nothing more than getting used to the apparatus becomes very probable from a scrutiny of the work from Schneider's laboratory. Whereas such a drop was found in eight out of his ten athletes, it appeared in only three out of seven non-athletes subjected to training. In each case, non-athletes were laboratory workers who, in addition to being subjected to more actual tests, were undoubtedly also already more familiar with metabolism apparatus to begin with. There is no doubt that a large cause for the uncertainty in this field lies in the difficulties inherent in the problem. In no studies on man has diet been rigidly controlled, in none has the period of observation been more than seven months, in none have metabolism tests been performed oftener than "occasionally" before, during, and after training; in none were other individuals living under identical conditions, though without exercise, being observed simultaneously to throw light on the nature and extent of spontaneous and uncontrollable factors. The present author's already cited observations on at first four, and later three dogs on a constant and controlled diet, with almost daily tests over a period of five years in which the animals were kept clean and free from parasites and only one animal exercised at a time while the others that served as controls were not used in other

experiments in the meantime, has impressed upon him the importance of extended tests if one is not to be misguided by the many "whims" of the basal metabolism, which we have not yet learned to understand. Particularly in "training studies" are these given opportunity for expression. We must not deceive ourselves by assuming that total metabolism studies have brought us to conclusions regarding the fundamental questions involved. Thus, as again most recently emphasized by Schneider and Foster (208), training may stimulate cellular activity, but the simultaneously gained improvement in relaxation may produce economies in oxygen consumption sufficient to mask these changes. It is also possible that muscle tonus in the *completely relaxed state* may at best play such a small rôle in determining the total basal metabolism that an appreciable muscle hypertrophy may go unnoticed. The observation by Schneider and Ring (210) that two of their subjects in training exhibited at once slight increases in the sitting, resting metabolism, and slight reductions in the basal metabolism, suggests such a possibility and may also explain why workers who paid less attention to securing absolutely basal conditions, reported rises due to training. Another possibility suggests itself. It is conceivable that training may induce economies in the functioning of certain internal organs sufficient to overshadow any increase in the oxygen requirements of the skeletal musculature.

Work metabolism. Work cost. The total amount of oxygen consumed during and until complete recovery after a work period less the resting metabolism of a corresponding length of time, is a measure of the energy expended by the body in the performance of the task in question. When this is converted into an appropriate unit, such as the Calory, and divided into the total work done, also expressed in Calories (1 kilogram meter = 0.0024 calorie), the quotient expressed as per cent is known as the net mechanical efficiency. Until the work of Hill and his collaborators emphasized the importance of the oxygen debt as part of the work cost, workers in this field accepted the oxygen consumption per minute during work as a measure of this cost. As Simonson (224, p. 815) points out, the older figures are essentially correct if, as is probably the case, they were taken during the "steady state" of long periods of work. From this viewpoint the older work, such as that of Zuntz, and Benedict and Cathcart, cited by Bainbridge et al. (9, pp. 22, 26) indicating the efficiency of experienced men on a bicycle ergometer to be from 5 to 13 per cent greater than that of inexperienced ones, is essentially dependable. Zuntz was also able to show that the efficiency of a dog in climb-

ing was improved by practice. In recent years, with methods taking cognizance of the oxygen debt, similar results were secured by Henderson et al. (101) on trained and untrained athletes, and by Seppölä et al. (216) on gymnasts of varying grades of experience. Gemmill et al. (78) have tabulated the findings of a number of workers on this problem. There is a great deal of evidence that this improvement is due entirely to better coördination. Dill et al. (50) have employed this fact in the development of a "skill index" in terms of oxygen requirements for a given task. In this sense *the improvements in mechanical efficiency which come with practice are really a measure of the effect of training on the central nervous system and not a measure of improved metabolism in the sense of more economical intracellular activity.* A poorly coördinated man consumes more oxygen because he is actually doing more work than the well coördinated man. With practice he develops the ability to circumvent this extra work.

The field of industrial hygiene, especially as it is developed in the German "Arbeitsphysiologie" movement, furnishes many illustrations of this phenomenon (Atzler et al., 6; Lehmann, 160). Often, weeks of practice are found necessary before successive repetition of a single manual operation yields constant work-cost values. And even after such stability is attained and the experiment in question has proceeded to other phases, a retesting of the original operation months later may disclose further economies (Lehmann, personal communication). Meyer (175) believes that the attainment of maximum efficiency in many cases awaits the increase in strength resulting from gradual changes in the muscles involved.

It is most important that this improvement in economy be recognized as improvement in skill and that it be not taken as a measure of the degree of training. Especially is this important in attempts to measure the work capacity or efficiency of other organs such as the heart. It is for this reason that the oxygen consumption is taken as the measure of work done rather than the external or technical work measured in foot pounds or kilogram meters, when the capacity of vital organs or of chemical equilibria, to meet work conditions is to be gauged. It would seem superfluous to bear at so great length on this point but for the fact that some present day workers have not yet recognized fully its significance in the interpretation of their findings. Abramson (1) has helped further to define the issue in an experiment which showed that improvement in skill is retained longer and depends more on native ability than improvement in strength and endurance. He concludes,

"Man lernt Radfahren einmal in seinem Leben, Kraft und Ausdauer müssen jedes Jahr wieder eingeübt werden."

Recovery. The recent experiments of Talbot et al. (235) and Gemmill et al. (77) on running, since they employed already familiar movements, showed no reduction in work cost as the individuals became better trained. Yet with training the subjects become able to do more and more work. This of course is due to many factors discussed elsewhere. Here, it is in order to point out the improvements in terms of "enhanced recovery," i.e., payment of the "oxygen debt." Simonson and Riesser (225) employed the lifting of a weight of 12.5 kgm. ten to twelve times upwards from shoulder height as test exercise. During four weeks of twice daily practice in which each of three subjects increased their ability to raise the weight from thirty times to sixty times at a session, the actual work cost of ten to twelve lifts remained constant. The training period was however marked by a shortening of the recovery period. More and more of the oxygen required was taken in during the actual work period leaving less of an "oxygen debt." From the empirically determined curve of oxygen consumption in the recovery period, Simonson derived a formula from which the "restitutions konstant" (*RK*) may be determined. In his formula $RK = \frac{1}{t} \ln \frac{\text{Cal } A}{\text{Cal } t'}$, Cal A is the total oxygen debt at the moment when exercise ends and Cal t the portion of the debt remaining after the elapse of time t, in practice three minutes, after the end of exercise. The thus secured coefficient he finds a useful expression for the fitness of the individual. In the training period above mentioned this *RK* increased from 0.33 to 0.54, 0.35 to 0.50, and 0.42 to 0.73 in his three subjects. Gottstein (84), Rosenblum (198), and Kagan and Kaplan (136) also observed that training is characterized by a greater O_2 absorption during work leaving less to be absorbed in recovery. Sargent's (202) ability to predict a runner's time in a race of any length after determining: 1, his oxygen cost for running 120 yards at various speeds; 2, his maximum oxygen debt; 3, his maximum oxygen absorption; and Herbst's (102) finding that

$$\frac{\text{maximum } O_2 \text{ absorption rate}}{\text{Bdy wt. in Kgm.}}$$

bears a linear relation to work capacity are of the same stripe and represent beautiful approaches to a mathematical evaluation of the cardiorespiratory mechanisms, all of them outgrowths of the fundamental

observations of Prof. A. V. Hill. (See also the calculations of Gemmill et al., 77.)

From this standpoint the greater abilities of the trained state are due, first to improved skill, i.e., training of the nervous system, and second, to the approximation of "cash payment" of the cost of work, i.e., training of the cardio-respiratory systems. To date there is no evidence of a more economical working of the muscle cell per se. There are many who speculate that training may in some way teach the muscle cell to oxidize more rapidly.

In the fact that fatigue decreases the ability to coördinate, we see another route by which the degree of training may indirectly influence work cost (Ilzhöfer, 129).

Respiratory quotient. The scattered observations on the *basal* RQ in training experiments indicate no change in the muscle cells' choice of fuel. The observations of a slowly rising basal RQ as reported by Dirken (51), Schenk and Stähler (204), is rightly attributed by the latter to the excessive increase in sugar consumption. Herxheimer (116, p. 726) is astounded by the success of candy concessions in the neighborhood of athletic stadia in Germany and finds in it objective evidence for the unusual desire among athletes in training to consume candy. That the American athlete does not distinguish himself in this way is probably due to the large consumption of sweets by the non-athletic population in America. Experiments to throw light on the blood insulin or sugar tolerance in and out of training might help to determine whether there is a more fundamental basis for these observations.

At work, the RQ of trained individuals is lower than that of the untrained, as shown by Bock et al. (24), Kagan and Kaplan (136), and Christensen (37). The last named worker and Bierring (22) also of Copenhagen, present good evidence that respiratory quotients of work equal to or exceeding 1.0 appear only in cases where the circulo-respiratory system is over-taxed and therefore they cease to reflect the nature of actual oxidative changes. Highly trained subjects are able to perform a huge amount of work without apparently overstepping these bounds. Thus Christensen's trained subjects produced 1920 kilogrammeters of work per minute on a bicycle ergometer, with an oxygen absorption rate of 4.7 liters, probably the highest oxygen absorption on record. Their RQs. never exceeded 0.95.

A number of workers, among them both Bock and Christensen, have shown that under conditions *seemingly* meeting the requirements of the "steady state," the RQ increases as the load increases and that at any

particular work-level measured by oxygen consumption, the RQ of untrained subjects is higher than that of trained ones. Bock et al. (24) believe that the mounting RQ in work signifies that the conversion of fats to carbohydrates is unable to keep up with the muscles' consumption of carbohydrates and that somehow with training this ability to change fats to carbohydrates is also increased. The Copenhagen group, on the other hand, doubt whether the differences in RQs. noted actually reflect differences in oxidative processes. They believe that the possibility of gradual loss of CO_2 from blood and tissues has not been satisfactorily ruled out. Analyses of arterial blood samples for CO_2 content will need to show constant values at all work levels before changes in the RQ can be taken to reflect truly "inner" changes.

Extremely low RQs. (0.55), persisting for hours *after* long and exhausting work in the untrained, reflect, no doubt, (139) a depletion of glycogen stores and their subsequent replenishment from other food principles in the absence of a sufficient carbohydrate intake. A laborer, whose diet was controlled at a moderately high caloric level in Szakall's (232) experiment, exhibited a higher and more constant basal RQ than did others who selected their diet independently.

Nitrogen, mineral, and water metabolism. There is a lamentable scarcity of long term metabolic studies designed to determine the course of metabolism other than that which is reflected in the gaseous exchanges. Toward the end of a month of training on a constant diet, Talbott et al. (235) found one gram less of nitrogen excreted per day than at the beginning of the experiment. This would be expected in the event of muscle hypertrophy. The daily creatinine output showed no changes. Their observations on PO_4, Cl, and SO_4 metabolism, though reflecting the immediate effects of exercise, throw no light on the training problem. The increase in water content of certain hypertrophied tissues observed by some workers would suggest an altered water metabolism. The problem has not been attacked from the angle of total water metabolism.

DIGESTIVE SYSTEM: *Submaxillary gland.* This was found by Donaldson (53) to be greatly increased in size in exercised rats.

Liver. From studies of organ weights, Külbs (153) on dogs, and Hatai (97) on rats, report an increase in liver size in trained animals. Donaldson (53) on rats reports a decrease, and Thörner (237), and Steinhaus et al. (229) on dogs, report no trend attributable to a long period of exercise.

EXCRETORY SYSTEM. *Kidney. Size.* Increased weight of the kid-

ney attributable to an active life of running was found by Külbs (153) (154) and Thörner (237) in the dog, and by Hatai (97) and Borovansky (27) in the rat. The observations on dogs conducted in the author's laboratory (229) failed to show increases due to running, but did show marked increase in kidney weight in dogs trained by swimming.

Function. There are no findings which may be taken to indicate chronic alterations in kidney function induced by exercise. The observation that lactic acid excretion as a result of exercise is reduced in training (164) (94), though not substantiated (118), is exactly what is to be expected in consequence of the lower production and better oxidation of lactic acid in a trained organism, and does not imply a raised kidney threshold to this substance. Knoll (143) reports that albuminuria following horseback riding, disappeared after several months of practice. His statement that the condition reappeared on days of extra heavy work as in breaking in a new horse, would indicate that these findings again need to be interpreted as concomitants of reduced work-cost, rather than due to an altered kidney.

ENDOCRINE SYSTEM. The *hypophysis* was found by Hatai (97) to be enlarged in male and reduced in female rats by exercise.

The *thyroid* gland is reported by Hatai (97) and Donaldson (53) to be reduced by exercise in the rat. Steinhaus et al. (229) found markedly larger thyroids in trained dogs. Bast et al. (11) found histologic evidence of hypersecretion in the thyroid of exhausted rabbits.

The *adrenal* gland is reported by Hatai (97) to be unchanged in the male but enlarged in the female rat by exercise. Donaldson (53) found it enlarged in both sexes. Steinhaus et al. (229) found it decreased in running and increased in swimming dogs.

There are no reports of organ-weights for the *pancreas*. There is clinical evidence (Lawrence, 157), that a moderate diabetic needs less insulin when exercising. Gerl and Hofmann (79) report similar observations and develop the theory that exercise stimulates the remaining islet tissue to greater activity. They believe that with training the pancreas of normal man responds with insulin secretion more promptly, so that the initial hyperglycemia of exercise ceases to appear. These views, though interesting, are in need of more incontestable, experimental support.

REPRODUCTIVE SYSTEM. *Size.* Hatai (97), Borovansky (27), and Donaldson (53) report increases in the size of rat gonads due to exercise. Steinhaus et al. (229) found the opposite in dogs.

Function. There have been numerous statistical studies such as

Casper (33), Runge (201), and Duntzer and Hellendall (54), which indicate that a very active athletic life is without effect on the normal functioning of the female reproductive organs in most cases. The only experimental study is that of Okuneva et al. (181) who devised a method for graphically recording movements of the uterus. They employed this method on Russian women in industry and found considerable displacement of the uterus when weights were lifted. With weights of 20 kgm. this downward displacement persisted for some time afterwards. By checking simultaneously the changes in rectal pressure they found that the uteral excursions were related directly to the changes in abdominal pressure. They believe that the high rate of menstrual disorders observed in these factory workers is thus explained. Hartman (93) presents some inconclusive data which indicate that an active life favors ovulation in the opossum.

OTHER ORGANS. Whereas Külbs (153) reports slightly larger *spleens* in exercised dogs, Hatai in rats (97) and Thörner in dogs (237) report reductions due to exercise. Steinhaus et al. (229) found no change due to running exercise, whereas in dogs which were made to swim, they found also a smaller spleen.

Hatai (97) reports the *thymus* of exercised rats to be larger than that of controls.

CENTRAL NERVOUS SYSTEM. *Mass.* The brain weight of exercised rats is reported by Hatai (97) as 4 per cent and by Donaldson (53) as 2 to 3 per cent heavier than that of their unexercised littermates. These workers found no difference in the weight of the spinal cord.

Coördination. Undoubtedly the greatest and most lasting changes which training induces in man and animal take place in the nervous system, namely, changes in behavior. Among these changes only those which manifest themselves in "muscle learnings" or improved coördination need enter this discussion. Objectively, these improvements have been measured in two ways. The increased mechanical efficiency or reduced work cost of the trained state have already been discussed. The other approach consists of analyzing the movements of athletes by the well known "slow-motion" film, in which as high as 200 exposures are taken per second. By this method, Jokl (131) (131a), and Knoll and Morenz (144) were able to show that the poor or untrained runner raised and lowered his center of gravity much more with each step than did the good runner. Even hurdling is executed by the expert with but very little raising of the center of gravity. A good runner's stride is longer, his trunk is bent more forward and rotates less, his arms move

more effectively to assist in the forward movement, and his legs move more evenly and strike the ground in front in such manner that the forward movement is checked as little as possible. Fenn (70) (71) has pioneered this field in America.

Higher processes. There have been many claims that training in some way improves the quality or functioning of brain tissue so that learning is facilitated. This was recently tested by Corey (40) on the rat's ability to learn to run a maze. The results were completely negative. Nor does the literature recording attempts to correlate muscular development and other indices of training with scholarship and character give encouragement for holding this view.

GROWTH AND SKELETON. Since muscle growth has already been discussed under the heading of muscle, only the skeletal aspects of growth and a few body-weight studies need be here considered.

In man it is an unsettled question as to whether the growth of long bones is accelerated or retarded by an active life. Thus some (Aron, 5; Arnold, 4) are of the opinion that exercise stimulates growth in girths and delays the attainment of full height in school children, while Kohlrausch (148) claims to have observed a growth stimulating effect on arm and leg lengths in students of physical education. He also cites the abnormally large left hands of famous bass viol players to be in harmony with his findings. The latter worker, seeking to unify all observations, develops the position that the pressure effect of exercise on the epiphyses of bones stimulates growth up to an optimal length and beyond this point retards growth. Accordingly, too little exercise might account for undersized development as well as for overshooting the mark.

Müller (178) reviews the earlier experiments on *animals* and reports an experiment on rats in which he skinned a leg and sewed it up under the skin. The tibia or radius of a leg thus inactivated for six weeks was regularly found to be 1 to 1½ mm. longer than its homolog of the active side. Friedländer and Thierse (74) compared the bones of a limb inactivated by a stiff bandage (dogs and rabbits) and by denervation (rabbits) with the homologous limb of the untreated side. They found lighter bones with higher water content and less mineral matter even in the dry weight, and rarefication (roentgenographically) in the inactivated limbs. These atrophic signs they attribute to a reduced blood supply due to less exercise. Further, they found the "inactivated" bones longer and slenderer with both roentenographic and histologic signs of a more actively growing epiphyseal line. These changes they

attribute to the absence of the normal stimulus to lateral growth exercised by pulling muscles at their points of attachment, and to the absence of the growth-slowing effect of pressure on the ends of long bones.

Mellanby (173) and Port (188) found that rickets developed more slowly and less severely in rats fed a diet deficient in vitamin D, if they were exercised while on this diet. Mellanby believes this is due to exercise making available every last bit of stored vitamin D.

The *growth* of rats as judged by increase in body-weight was studied by Ylanan (251) and Price-Jones (189). Both found that very strenuous exercise markedly retards growth in spite of the maintenance of good nutrition. The former noted in addition that moderately exercised animals grew faster than totally unexercised ones. Borovansky (27) found that moderate exercise increased the weight of rats but was without effect on body length.

A number of workers, Baetzner (8), Pitzen (185), Heiss (99) (100), and Hora (126), have reported changes in the skeleton of highly specialized athletes as observed by x-ray and from surgical material. These include: 1, enlarged bony processes marking origins and insertions of the muscles most used; 2, irregular extensions of the articular surfaces as in beginning arthritis deformans; 3, accessory bones of the sesamoid type, particularly in the olecranon region of the arms of wrestlers and in the patellar ligament of sprinters; 4, foreign bodies, probably cartilaginous, within the joint capsule; 5, degenerative changes of the articular cartilage evidenced by shredding, chipping, softening, splitting, and dissolution, also inflammatory proliferation of cartilage and bone. These changes, it is emphasized, are not the result of a single injury, as for example the "baseball pitcher's elbow" described by Kirby (140), but rather due to an accumulation of minor insults imposed by the incessant pounding on certain joint surfaces, characteristic of a highly specialized sport. Baetzner cites illustrations to support his view that the torn lemniscus common in the knee joint of soccer players is predisposed by previous injury of this kind to the cartilage. Hora found that most of the bony changes in soccer players were found in the feet. He believes that constitutional factors determine whether these changes shall lead to mere thickening of the bone or to more definitely pathological changes.

Göcke (82) subjected excised human vertebrae to often repeated (1000–4000 times) light hammer blows. The deteriorating effect of the hammering displayed itself in lowered tensile strength of the bones.

His contention, that the differing degrees of resistance manifested by the bones of various individuals may be related to their "constitutional type," is, as he admits, far from established by his limited amount of data. Knoll (143a, b, c) has challenged the Baetzner concept of "Sportschäden," contending that in most cases the joint and bone changes may be traced to some actual accident to the joint and that where such an explanation is not to be found the change is better interpreted as an adaptation rather than an injury. Further, the importance of making equally minute observations on a large body of nonathletic material is emphasized by Knoll's casual findings of bony growths, similar to those described by Baetzner, in individuals who had never engaged in sports. Heiss (100) observed students of physical education over a period of three years. He found that certain already existing bony processes increased and new ones, similarly attributable to the activity program of these students, made their appearance during the period of observation. More observations of this type are needed to settle the question.

ATHLETIC TYPES. From an anthropometric study of 515 high grade athletes representing fifteen different athletic specialties, Kohlrausch (149) finds justification for associating body-form with athletic prowess. He recognizes, of course, many other determining factors which neither the tape nor the camera can record, which must account for not uncommon exceptions in any classification built on a limited group of measurements. To a great extent these measured characteristics are the *cause* rather than the *result* of athletic performance, yet there are also numerous signs of *results*. Such, *for example*, are obviously the heavy musculature of the shoulders in "turners" and boxers. Kohlrausch (149) believes, however, that other characteristics such as the bow-legs of soccer players, a peculiar position of the clavicles and a thick layer of subcutaneous fat in swimmers, as well as spinal curves characteristic of boxers, skiers, wrestlers, cyclists, and soccer players (146) are also chronic changes due to long participation in a single sport.

CLOSING STATEMENT

Exercise increases the capacity of the organism to perform work. Lindhard (166) recognizes improvements in *strength*, in *endurance*, and in *sureness or perfection* of movement and attributes them *in general* to changes in the muscular system, respiro-circulatory system, and nervous systems, respectively. Further analysis discloses an interlocking division of responsibilities.

Increase in *strength* is no doubt primarily associated with the hypertrophy of muscle in which largely the sarcoplasm participates. We know too little of the way in which chemical energy is transformed into mechanical energy in the muscle to speculate on how the observed changes in muscle chemistry contribute to the increase of strength. Nor can we estimate what fraction of the increase in strength should be attributed to more complete subjugation of all muscle cells to the voluntary processes. The unusual feats of strength which can be performed by people of ordinary development when in hypnotic states or when excited, suggest that strength may also in part be learned. Morpurgo's observation (177) that the hypertrophied muscle contains fewer cells of very small diameter may be interpreted in the same way.

Endurance, or the postponement of fatigue, is a measure of the organism's ability to balance catabolic with appropriate anabolic processes. Primarily, this means a sufficient supply of oxygen, and secondarily, a food supply. If we follow Lundsgaard (both Meyerhof (175a) and Hill (120a) have recently presented the total picture admirably) in seeking in the break-down of phosphocreatine and its immediate resynthesis at the expense of a glycolytic process, the chemical changes most intimately related to muscle mechanics, we may postulate the following possible causes of fatigue: 1, depletion of the phosphocreatine store as by loss of one or both of its breakdown products; 2, failure of the resynthesis process due to some limitation being set on the production of lactic acid which most commonly is probably due to the accumulation of lactic acid and therefore due to 3, inability to oxidize lactic acid promptly due to a shortage of oxygen. The lactic acid thus accumulated enters the circulation and causes 4, disturbances in CO_2 carrying power of the blood, in the respiratory center and in vasomotor regulation which an increased circulation can only temporarily compensate; 5, failure of the circulatory and respiratory system to meet these demands.

Training increases endurance by meeting these problems in the reverse order. The increased return of venous blood brought on by the pumping action of active muscles fills the heart more completely which in accord with the "law of the heart," induces stronger systoles. Oft repeated, this leads to cardiac hypertrophy with corresponding greater stroke-volume, resting minute-volume, and slower pulse rate. The faster circulation of the blood results in fragmentation of older corpuscles both red and white, and a consequent stimulation of the corpuscle producing tissues. The blood corpuscles are thus "trimmed" for

greater service. A greater resting minute-volume, augmented by the return flow as soon as exercise begins, carries much greater supplies of oxygen to the active tissues thus providing for the disposition of lactic acid *at its source* and preventing its entering the circulation in quantities large enough to disturb other equilibria. Since it has been established that in the presence of sufficient oxygen, phosphocreatin may be directly resynthesized *without lactic acid formation* (166a) the possibility suggests itself that the highly perfected oxygen transport of the trained individual may provide the conditions necessary for more of this direct resynthesis, thus reducing the need for the indirect process involving the formation of lactic acid which, if not less efficient, is at least an extra burden. The finding of an increased glycogen content in an intermediate stage of training and its subsequent disappearance in highly trained dogs (190) would take on significance in this light.

If endurance is the result of a balance between the catabolic and anabolic processes the facilitation of the anabolic processes occasioned by training must of course be measured in terms of the catabolic processes which they can compensate. In our considerations these are expressed in terms of the intensity and duration of the exercise or work performed. Most persons have a high degree of endurance for walking but as the required work increases, more and more find their stage of training insufficient to maintain this balance and they begin to show one or another sign of fatigue. Thus even the most highly trained reaches his limit if the exercise is sufficiently strenuous. In the same sense a person is fully trained to one level of work and only partially trained to a higher level. The speed at which muscles can operate is such that the maximum demands for oxygen which they are able to create cannot be met, no matter how highly trained the individual may be. In this event oxygen transport ability is probably compensated or, at very high rates of work, even replaced by lactic acid-buffering ability as the limiting factor in endurance. Improvements in this property have been observed in the increased alkali reserve and called a form of chemical training (64).

To bring about the many cardiac, vasomotor, and respiratory adjustments a great burden is placed on the nervous system, particularly the autonomic portions. Undoubtedly during exercise these adjustments are mainly due to sympathetic activity. Conversely a number of workers have found in the signs of training apparent at rest, reason to assume the development of vagotonia (203) as a sort of reaction to the sympathicotonia of work.

Perfection of movement is the most prominent result of training. It is also the most specific. Thus endurance may be developed by boxing, swimming, or running, but the finesse of boxing can be perfected only by the practice of germain movements. Zuntz found that a dog trained to walking on the level was not trained for walking on an incline. A most important by-product of the development of skill is the economy of effort which the more purposeful use of the muscles entails, thus reducing the total load and at once postponing fatigue.

Professor Orbeli of Leningrad recently expressed to the author his opinion that a large fraction of the trained state is due to the establishment of conditioned reflexes involving adjustments through the autonomic nervous system. Not only does his conception include such reflexes as the acceleration of heart and respiratory rate in anticipation or at the beginning of an athletic contest, but he would look also for changes in the muscle cell's ability to adjust to its milieu and in the reflex centers themselves. Professor Orbeli's observations on the influence of sympathetic nerves over the composition of muscle tissues and the activity of various portions of the reflex arc (Kunstman, 155a) lend support to such a position. Professor Brücke has recently (30a) prepared a summary of Orbeli's findings which hitherto were inaccessible to non-Russian readers.

In addition to these changes which directly or indirectly increase the capacity for work, there are *other effects* of exercise which must be considered as either meaningless at present, or actually deleterious. Among these may be listed certain changes in the leucocyte and thrombocyte picture, modifications in the growth of bones, and joint changes. The problem of chronic fatigue and overtraining also would fall in this class and is deserving of more careful investigation. Until we know more of the relation of endocrine glands to the performance of work, the scattered observations recording altered size in these organs shall also remain meaningless.

The recent observations of Lehmann and Szakall (161) indicating that exposure to ultra-violet radiation induces many of the changes usually found in training, raises the question as to how much of the supposed training picture is due to the light factor when athletes train outdoors.

In rats Donaldson (53) found none of the exercise changes to be *inheritable* even after their experimental induction through seven successive generations.

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